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TABLE OF CONTENTS

Uses of Epidemiology J. N. MORRIS, M.R.C.P., D.P.H. 395
Assessment of Adrenocortical Function in Cases of Pituitary Tumour H. J. CROW, M.B. 401
Peripheral Arterial Embolism R. P. JEPSON, M.B., F.R.C.S. 405
Ocular Nerve Palsy with Severe Headache in Diabetics W. P. U. JACKSON, M.D., M.R.C.P., D.C.H. 408
Neurosis in General Practice J. C. E. POUGHER, M.B. 409
Insulin Zinc Suspension in Childhood Diabetes O. H. WOLFF, M.D., M.R.C.P., D.C.H., and T. G. MADDISON, M.D., M.R.A.C.P. 413
Trichophyton Sulphureum Ringworm DENIS SHARVILL, M.R.C.P. 415
Treatment of Ascariasis in Children with Piperazine Adipate M. HANNA, M.D., D.Ch., and A. H. SHEHATA, M.D., D.Ch. 417

MEDICAL MEMORANDA

Ferrous Sulphate Poisoning with Gross Stricture of Stomach. J. A. SHEPHERD, M.D., Ch.M., F.R.C.S.Ed. 418
Case of Priapism. W. J. FRASER, M.B., F.R.C.S.Ed. 419

BOOK REVIEWS 420

REFRESHER COURSE

Acute Alcoholic Poisoning. J. A. IMRIE, M.D., F.R.C.S.Ed. 428

GENERAL ARTICLES AND NEWS

Uganda and Great Ormond Street. BERNARD SCHLESINGER, M.D., F.R.C.P. 430
ROLE OF MIDWIFE, FAMILY PRACTITIONER, AND SPECIALIST IN NORMAL LABOUR 431
PREPARATIONS AND APPLIANCES 432
NOVA ET VETERA 432
MEDICO-LEGAL 441
UNIVERSITIES AND COLLEGES 441
VITAL STATISTICS 442
MEDICAL NEWS 444
QUESTIONS AND COMMENTS 446

OBITUARY

Sir Reginald Bond, K.C.B., M.B., F.R.C.P., F.R.C.S.Ed., D.P.H. 439
J. D. Martin-Jones, M.D., D.O.M.S. 440
Moritz Blumberg, M.D. 440
J. P. Quinn, M.C., M.B., D.P.H. 441
John Sexton, M.B. 441

LEADING ARTICLES

Breath-holding Attacks 422
Dietary Protein in Acute Nephritis 423

ANNOTATIONS

Home and Clinic Treatment of Tuberculosis 424
Endogenous Depression in Children 425
Radium Treatment of Deafness in Children 426
Citrate Intoxication 426
Hyperglycaemia and Visual Disturbances 427
Visit of Russian Doctors 427

SUPPLEMENT

Full Contents on First Page of Supplement

Scope of the District Nursing Service 47
Nyasaland Branch 49
N.O.T.B. Association 49
N.A.L.G.O. Golden Jubilee 49
Correspondence:
Appointed Factory Doctor. J. G. HAGAN, M.B. 49
Trainee Assistants' Car Expenses. M. Dunsby, M.B. 49
Life as a National Service M.O. N. L. EDMOND, M.B. 49
Tax Relief on Capital Expenditure. A. J. O'FRIEL, M.B. 50
Cost of National Health Service. H. C. CRAVEN VEITCH, M.R.C.S. 50
Clinical Work and M.O.H. H. L. SETTLE, M.D. 50

CORRESPONDENCE

Acute Leukaemia. K. J. GURLING, M.D. 433
Replacement Transfusion. C. C. BOWLEY, M.B., and others 434
New Look at the Curriculum. J. STEPHEN 434
Tonsillectomy. E. H. RAINER, F.R.C.S.Ed.; R. J. HAMER HODGES, F.F.A. R.C.S.; J. CROOKS, F.R.C.S. 434
Snake-bite. E. R. S. HOOPER, F.F.A. R.C.S. 435
Diabetes and Pregnancy. M. I. DRURY, M.D. 435
Acute Hepatic Failure. G. E. FFRENCH, M.D. 435
Antibiotics. D. CLARKE, M.B. 436
Penicillin. R. G. ORR, M.B.; C. B. HEALD, F.R.C.P. 436
Labelling the Container. H. S. M MAXWELL, L.R.C.P.Ed.; G. N. L. GODBER, M.B. 436
Spectacles. J. KEYMS, M.D. 436
Physique of Children. R. W. PARNELL, D.M. 437
Comforters. D. W. WINNICOTT, F.R.C.P. 437
Prophylactic Packets. G. G. THYNE, M.R.C.S. 437
Activity of Piperazine. O. D. STANDEN, M.Sc., and others 437
Opportunities for Medical Practice. C. H. DICKSON, M.B. 438
Cancer. R. STEIN-WERBLOWSKY, M.D. 438
Visit of Russian Doctors. L. CROME, M.R.C.P.Ed. 438
A.I.D. N. C. HYPHER, M.R.C.S. 439
Whipple's Disease. P. FARNAN, M.B., and R. A. GOODBODY, M.D. 439

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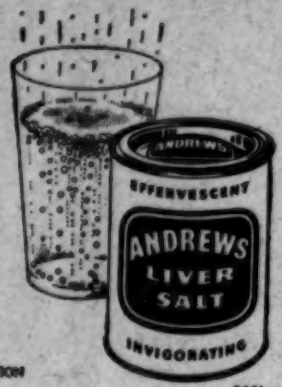

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY AUGUST 13 1955

USES OF EPIDEMIOLOGY*

BY

J. N. MORRIS, M.R.C.P., D.P.H.

Social Medicine Research Unit, Medical Research Council

Until about 1900 death rates in middle age were high and worsening (Fig. 1A), but about the turn of the century sanitary reform began to show results in this age group. Mortality rates for both men and women began to fall, and they continued to fall fairly sharply until the 1920s. Then something happened. Female mortality maintained its downward course; but the reduction of male mortality slackened and almost stopped. One result of this is that death rates for these men, which were about 10% higher than for women a hundred years ago, and about 33% higher after the first world war, are now 90% higher. What happened? As we now know, many strange things were happening, and are reflected, in the vital statistics of the interwar years. The most important was the emergence from obscurity of three diseases, particularly affecting males, and very common in middle age: duodenal ulcer, cancer of the bronchus, and "coronary thrombosis." The first of these is mainly important as a cause of morbidity; the other two are now major causes of death, killing annually over 20,000 middle-aged men. Fig. 1B shows the figures for 1928–53, and the contribution of these two diseases to the course of mortality: the trend among men is very different without them.

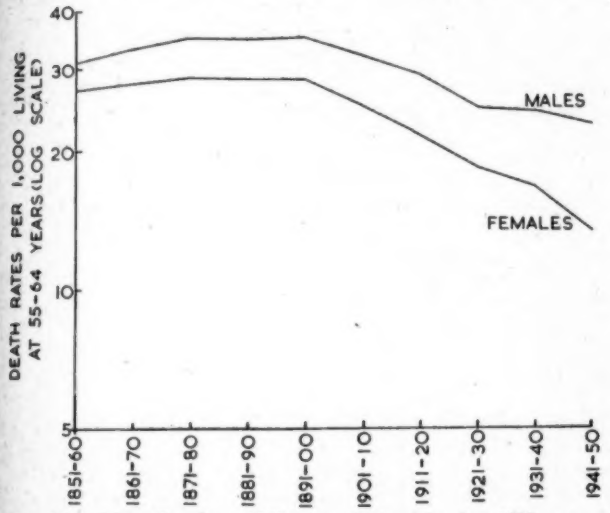

FIG. 1A.—Mortality in middle age during the last 100 years. England and Wales.[21] All causes.

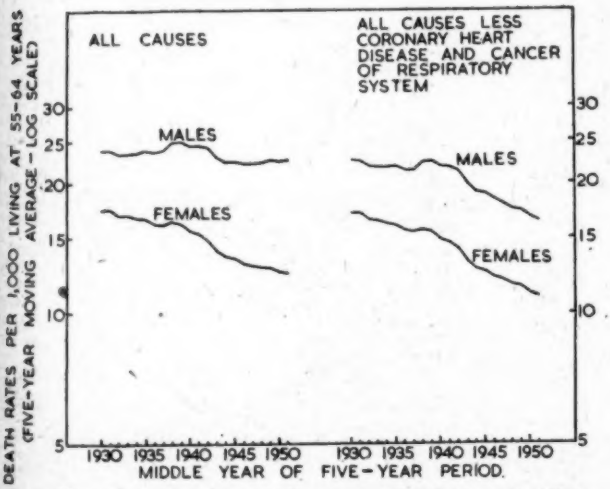

FIG. 1B.—Mortality in middle age. England and Wales. 1928–53.[21 26]

Figs. 1A and B illustrate one use of epidemiology—in historical study. But first let me explain that what I am speaking of is the study of health and disease of populations and groups, the epidemiology of which Farr, Snow, and Goldberger are the masters. By contrast with clinical medicine the unit of study in epidemiology is the group, not the individual: deaths, or any other event, are studied only if information can be obtained, or inferred, about the group in which the events occurred. The clinician deals with *cases*. The epidemiologist deals with cases *in their population*. He may start with a population and seek out the cases in it; or start with cases and refer them back to a population, or what can be taken to represent a population. But always the epidemiologist ends up with some estimate of $\frac{\text{cases}}{\text{population}}$. In consequence he can sometimes ask questions which the clinician may also ask, and get better or different information in reply. Sometimes he can ask questions that cannot be asked in clinical work at all. He can, for example, calculate the rates of occurrence, or frequency, of phenomena in the population—such as the deaths, from all and from particular causes, per 1,000 aged 55–64, a hundred years ago and now, to make possible the kind of comparison shown in Figs. 1A and B.

In this paper I am considering epidemiology as a procedure for finding things out, of asking questions, and of getting answers that raise further questions—that is, as a *method*—and I will have less time to consider the *results*, the information, obtained in reply. I shall confine myself to the non-infectious diseases, and try to illustrate them mostly from investigations carried out from the Social Medicine Research Unit, or with material worked up in that unit. Seven "uses" of epidemiology are described—different ways of looking at epidemiological data, or applications of the method.

*Read in opening a discussion at the Section of Preventive Medicine and Infectious Diseases at the Annual Meeting of the British Medical Association, Glasgow, 1954, and since expanded.

I. Historical

Historical statements made in medicine are of two broad kinds. The first describe the *decline* of infections, for example, and of nutritional deficiencies, and the main trends are usually very obvious. The others raise problems about the possible *increase* of various disorders, which is quite another matter. The questions usually put ("Have disk syndromes become commoner?" for example) are bedevilled by uncertainty about diagnosis and nomenclature in the past, and the lack of quantitative estimates of frequency at any time: How many cases occurred annually per 1,000 men, aged *x*, in the 1930s and in the early 1950s? In such problems as the frequency of psychoneuroses, historical questions, which are often asked, are hopeless of direct answer; but even in disorders like leukaemia, urinary cancer or cerebral tumour, subarachnoid haemorrhage, dissecting aneurysm, and the collagen diseases, it is exceedingly difficult to estimate how much a recent apparent increase reflects a *true* increase of disease, and how much it is the product merely of better recognition and greater availability of diagnostic services, etc. Such questions are clearly important because the role of environmental factors in aetiology, and of recent social change which may be associated with the increase, arises. As a result of a great deal of work, the increase of duodenal ulcer, cancer of the bronchus, and coronary heart disease must now be accepted as a working hypothesis and guide to environmental study.

History in the Making

Epidemiology may further be defined as the *study of health and disease of populations in relation to their environment and ways of living.* In a society that is changing as rapidly as our own, epidemiology has an important duty to observe contemporary social movements for their impact on the health of the population, and to try to assess where we are making progress and where falling back—an activity in line with the classic descriptions of famine and pestilence, of the relations of health and disease to social dislocations, wars, and crises. What are the public health implications of the 1,000 extra motor-vehicles a day?; the modern distribution of poverty so different from the 1930s?; the sophistication of foods?; the rising consumption of sugar, our astonishing taste for sweets?; the derationing of fats?; more smoking in women?; more married women going out to work?; less physical activity in work and more bodily sloth generally?; multiple chemical and physical exposures, known and potentially hazardous?; the prodigious increase of medical treatments?; the 11-plus examination?; still increasing urbanization and suburbanization?; the rapid creation of new towns?; smokeless zones (still with sulphur)?; the building of new power stations? And what can we learn from other indicators of community health: crime, for example—the ups and downs of juvenile delinquency, and the apparent increase of sex crimes and of crimes of violence during a period when so much other crime is decreasing?

Some of these questions are being studied, some cannot yet be framed in scientific terms; but parts at least of some could be better tackled than they are. And there are even more fundamental problems in our society; perhaps epidemiology with its concern for woods rather than trees, its special ability to isolate major characteristics for study, can simplify the issues and usefully raise some bold questions about these, too. Indices of health are available, and their quality is improving, although many more are needed, particularly in "mental health."

Looking Ahead

For many the main interest of history is the light it can throw on the future. Vital statistics is better placed than most disciplines to forecast—for example, the whole population of old people of the second half of the century are already born and are leading their lives under the conditions we know. Fig. 1A can therefore be projected ahead, if only with wide margins of confidence. What seems to be keeping the male death rate even as moderately satisfactory as it is now is the balancing of those diseases which are increasing (such as "coronary thrombosis") by those which are declining (tuberculosis and other infections). If the infectious diseases begin to reach some minimum before the *modern* epidemics are brought under control, or if their decline is halted, and if the large group of conditions which are relatively static (cancer of the stomach, cerebrovascular disease, etc.) do not show improvements in the meanwhile, the overall middle-aged male death rate will actually begin to rise. One consequence of this would be that the population of old people in the future will consist more and more of solitary old women (whatever the increasing popularity of marriage during recent years). The current trend of mortality in middle-aged males is the most striking feature of Western vital statistics. Very interestingly—another kind of epidemiological comparison—the situation is better in Scandinavia than in the English-speaking world, as illustrated by figures like these:

Mortality per 1,000 Aged 55–64 from All Causes. (Mean of rates for separate countries. Latest available year).

	Males	Females
Scotland, England and Wales, Canada, U.S.A., New Zealand, Australia	22·3	12·9
Norway, Sweden, Denmark	13·9	10·5

Searching questions need to be asked in this kind of situation. A first "reconnaisance" suggests that there is no simple answer—all these populations, for example, have high living standards and nutritional levels.

II. Community Diagnosis

Epidemiology provides the facts about community health; it describes the nature and relative size of the problems to be dealt with, and "maps" are produced of such scales as are required or possible. Results are sometimes surprising—at any rate in contrast with the type of problem of which there is general awareness and concern in the public health movement. Over 10% of sickness absence in male industrial workers in 1951 was ascribed to "bronchitis" (16 million days). "Psychological" disorders accounted for more than 13 million days;

TABLE I.—*First Reproductive "Cycle" in a Scottish City*[3 4 5 26 33]

Findings in Married Women	Social Class of Husband		
	I & II	III	IV & V
Physique of Women—Height			
Per cent. 5 ft. 1 in. (155 cm.) or smaller	12	24	28
Intelligence*			
Per cent. above average on matrix test	80	42	26
Education			
Per cent. leaving school over minimum age	56	14	3
Housing			
Per cent. living more than 2 per room	2	7	15
Family Budget*†			
Average weekly income (after compulsory deductions)	150s.	129s.	119s.
Nutrition*			
Calcium intake (mg./day)	1,219	1,071	868
Animal protein intake (g./day)	48·6	44·0	40·4
Reproduction			
Per cent. under 20 years old	2	11	17
Per cent. 30 years old or over	22	10	7
Per cent. pre-nuptial conceptions	15	24	37
Per cent. babies 5½ lb. (2·5 kg.) or less at birth	4	8	10
Child Care			
Per cent. fully breast-feeding at 3 months*	60	37	29
Per cent. "potting" regularly at end of first month*	72	49	28

This Table deals with local married primigravidae "booked" for the Aberdeen Maternity Hospital, 1948–52; and includes 85–90% of all who were eligible. Data are for periods varying from one year (818 cases) to five years (4,365 cases). Social classes I and II include the professions and business; class III are the skilled workers; IV and V the semi-skilled and unskilled workers.

Items * are for samples of the total.

† Clerical workers in social class III are included with classes I and II for Family Budget only. For other reasons, also, the sample of classes I and II for Budgets was not altogether satisfactory.

gastric and duodenal ailments for over 11 million, "rheumatism and arthritis" for over 11 million.[15]

Usually, however, we are concerned with the distribution of phenomena, and not merely their totals. Such distributions are firstly in terms of age and sex (race or colour, where applicable), economic status, and so on. Table I is an example of a social-economic distribution in relation

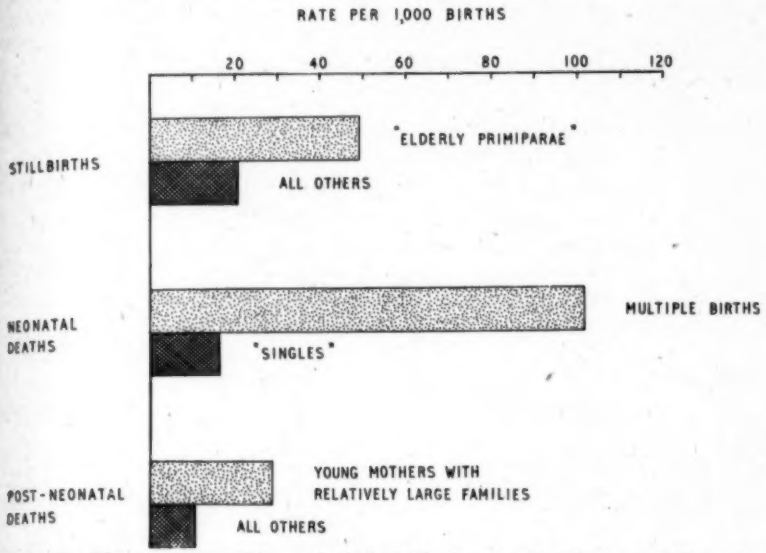

FIG. 2.—Three groups with particularly high foetal and infant mortality rates. England and Wales. 1949.[19]

to primigravidae in Aberdeen. It shows some interesting similarities, as in nutrition, and the remarkable differences that still remain between the social classes in "capital" goods like housing and education (in these early days of the Welfare State). There is a wide range of reproductive performance in this relatively homogeneous town. Such demonstration of inequalities between groups is a standard function of epidemiology, and it can be put to many uses—for example, in the same field as Table I, to identify "*vulnerable groups*" meriting special attention by health services (Fig. 2).

III. The Individual's Chances

The risks to the individual—or at any rate their order of magnitude—of suffering an accident as a schoolboy cyclist or an elderly pedestrian, of developing leukaemia

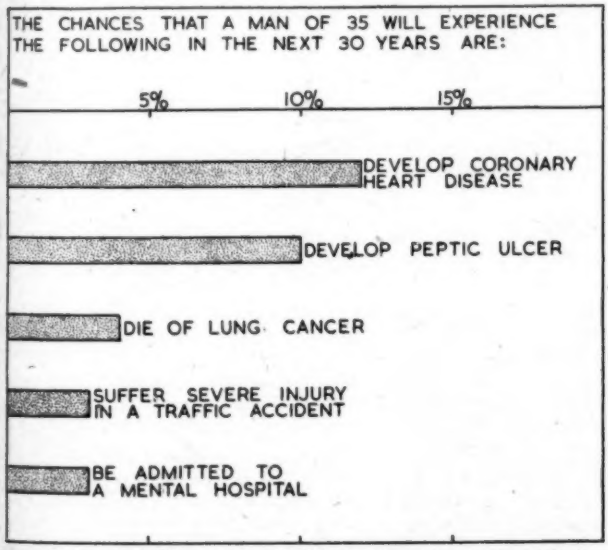
THE CHANCES THAT A MAN OF 35 WILL EXPERIENCE THE FOLLOWING IN THE NEXT 30 YEARS ARE:
5%
10%
15%
DEVELOP CORONARY HEART DISEASE
DEVELOP PEPTIC ULCER
DIE OF LUNG CANCER
SUFFER SEVERE INJURY IN A TRAFFIC ACCIDENT
BE ADMITTED TO A MENTAL HOSPITAL

FIG. 3.—The middle-aged man's risks to-day. England and Wales. Rough estimates.[7 11 12 16 20 21 24 25]

for a radiologist, of producing malformation from rubella or breast cancer from chronic mastitis, can be estimated only if the experience of whole populations of individuals is known and the relevant averages can thus be calculated. Fig. 3 uses the method of the life-table, an easy and rather neglected technique, to give a rough idea of the "risks" the average male in England and Wales now runs during his middle age, and it complements the picture of Figs. 1A and 1B. It is in the light of something like a one-in-eight chance of suffering from coronary heart disease, or one-in-ten from peptic ulcer, that the use of such terms as "epidemic" have their warrant. About 33% of men reaching 35 now die before they reach 65, compared with just over 20% of women. This approach is likely to become increasingly useful as forward-looking "prospective" studies are initiated, for example, to try to learn something about the differences made to middle-age mortality by different ways of living.

IV. Operational Research

The study of community health services—how they are working, what needs they are serving and how well, what they ought to be doing—is a slowly developing branch of social medicine little speeded by the war-time successes in rather different fields. Table II gives a few examples of simple analyses, using epidemiological methods, and the kind of questions (rather than answers) that emerge.

Why has the introduction of the National Health Service, in which for the first time every child has, or can have, a general practitioner, made so little difference to the school health service (Table II, A)? What are the appropriate roles to-day of school doctor and G.P.? How much "family medicine" can the general practitioner do if the children are treated elsewhere?

Is there enough "serious" medicine to maintain keen clinical interest in general practice; how is the work divided between "serious" and other problems (Table II, B)?

Since most attendances at these large and representative industrial medical officers' clinics (Table II, C) seem to be for "industrial" reasons, who, it may be asked, does the industrial medicine in the great majority of factories and other work-places where there is little or no industrial health service? What are the different elements in industrial

TABLE II.—*Working of Health Services*

A. *Treatment of Minor Ailments by School Health Service.* Before and after the National Health Service

Year	No. of Pupils	No. of Defects Treated at School Clinics
1947	5,034,275	1,190,754
1952–3	6,088,000	1,154,467

B. "*Serious*" *Clinical Medicine in a General Practice.*[2 28] During one year, 1949–50.

Age	Frequency of Serious Problems per 100 Persons	Proportion these formed of all the Doctor's Work with Age Group
0–14	22	20%
15–44	23	34%
45–64	41	55%
65+	83	76%
All ages	32	43%

C. *Functions of Occupational Health Service*, 1951.[28] Analysis of Sample Attendances at 12 Industrial Medical Officers' Clinics.

No. of Attendances in year	1,952
Proportion for "occupational reasons"	79%
" " "non-occupational reasons"	21%

D. *Impact of a New Therapy.*[22 23] Death rates per million from diabetes at 20–35 years of age. Males.

Social Class	1921–3	1930–
I and II	64	26
III	50	25
IV and V	46	35

medicine (carried out on the shop floor as well as in the clinic), and what is their relative importance, so that priorities for early advance can be planned ?

The diabetes figures (Table II, D) show that social classes I and II did much better with the introduction of insulin than classes IV and V (this is seen throughout " young " diabetes). How are the benefits of anticoagulants being distributed to-day, or of the new cardiac surgery ? Differences are, I fancy, more likely to be regional and local than related to " social class." And tonsillectomy ? Is Glover's fantastic tale[16] still true to-day ? Do children in Leeds, Leicester, and Exeter still run three times the risk of losing their tonsils as do the children of Manchester, Bradford, and Gloucester ? (And do these differences affect the children who most need to have their tonsils removed ?) In how many other examples of medical, obstetric, or dental care would such *community* comparisons stimulate fresh *clinical* thinking ?

Housing policy, pursuing the figures in Table I, evidently does not mean in the comparatively prosperous city of Aberdeen, little affected by bombing, that young people of any social class are finding it at all easy to start a home of their own (Fig. 4). Half of all families in 1951 were sharing

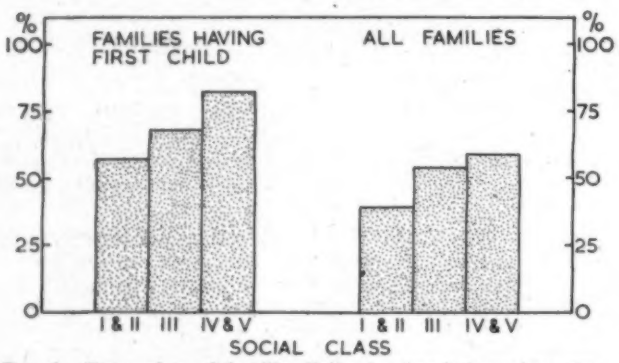

FIG. 4.—Proportion of families living in shared houses or flats. Aberdeen. 1951.[21]

dwellings. These housing figures are an illustration of the value of trying to base " operational research " about social services on populations : the idea of the *human needs* the services are and should be meeting at once becomes important. (Not that the assessment of " needs " is at all easy : so often " demand " is revealed—? created—by supply. However, in the health services—school, maternity and child welfare, appointed factory doctor—which were established to meet needs that certainly have since changed and may have lessened, a reassessment of the present situation is urgent. My private notion is that the Central Health Services Council might be armed with a research secretariat ; otherwise I see no prospect of having enough " operational research " carried out.)

V. Completing the Clinical Picture

The most obvious example of this function is the contribution of the epidemiological method in determining the sex and age incidence of disease. The calculation of accurate age-specific rates showing, for instance, that cancer of the ovary, and possibly of the breast, reach peak frequency late in middle age is of course a help in understanding these conditions, as are the relations with parity. But it is possible to go further. Epidemiology, being by definition concerned with all ascertainable cases in a population, often produces *different* pictures of disease from those derived only from hospitals, for example. Thus half or more of the deaths of men from coronary heart disease in middle age (56% here) seem to occur in the first few days of the first clinical attack of " coronary thrombosis " (Fig. 5). A quite incomplete picture of coronary heart disease must result if many of these cases are excluded. But often these deaths are " sudden," known only to the general practitioner and the coroner's pathologist. Special efforts are therefore needed to discover them, and, dependent on the success of such efforts, so may any picture presented of prognosis in this disease, of survival, and of the results of new treatments be very considerably modified.

The same is probably true at the other end of the spectrum : to get an idea of how much there is of *mild* ischaemic heart disease, minor and maybe atypical, reliance cannot be placed on the cases that happen to turn up in a particular practice or out-patient department, but an inclusive and extensive study is needed. (This principle is made use of in " screening " surveys to detect early subclinical disease. Thus detected, as in diabetes, progression may be halted, and the surveys are thus a measure of control or prevention.)

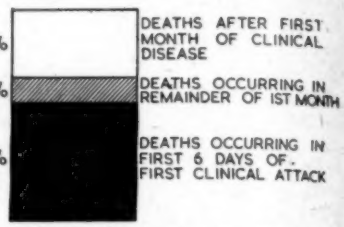
32%
12%
56%
DEATHS AFTER FIRST MONTH OF CLINICAL DISEASE
DEATHS OCCURRING IN REMAINDER OF 1ST MONTH
DEATHS OCCURRING IN FIRST 6 DAYS OF FIRST CLINICAL ATTACK

FIG. 5.—Deaths from coronary heart disease during middle age: Relation to first clinical attack. Male medical practitioners, 40–64 years. 1940–52. There were 136 deaths in 13 years.[20 29]

In brief, studies of the natural history of disease will be more complete and correctly proportioned if based on *all* the cases satisfying specified diagnostic criteria occurring in a defined population. Pneumoconiosis, byssinosis, rheumatoid arthritis, and nutritional disorders such as anaemia come to mind in this context.[6 13 27]

VI. Identification of Syndromes

This use again relates directly to clinical medicine. Broad descriptive clinical and pathological categories often include very different elements. Their different statistical distribution, and their different behaviour among the population, may make it possible to distinguish such elements from each other, and thus help to identify characteristic syndromes. Consider the mortality from " peptic ulcer " in *1921–3* (Fig. 6). Clearly there were at least two conditions to be

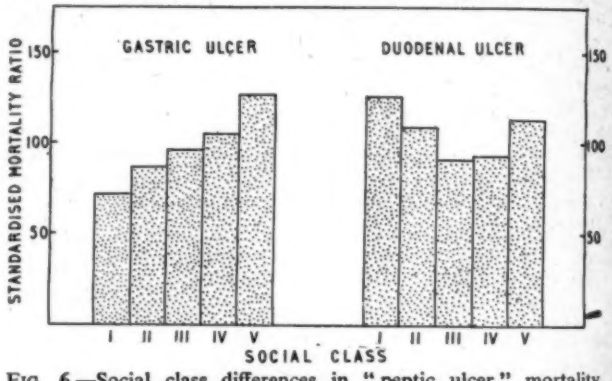

FIG. 6.—Social class differences in " peptic ulcer " mortality. Males. England and Wales. 1921–3.[22]

studied—conditions with possibly different causes. My own main interest in this field is in trying to disentangle coronary heart disease from coronary atheroma, by study of their different distributions in the population to-day, and their different histories in the past 40 years.[17] Table III illustrates again from cardiovascular disease. The common lumping together of coronary and cerebrovascular lesions as " atherosclerosis " is not very strongly justified in clinical or pathological terms. Nor do the two conditions always behave similarly epidemiologically : the recent vital statistics are quite different ; and this small experience among doctors (Table III) is interesting. The natural history of conditions as *group* phenomena may thus help to define syndromes. The vast unknown field of chronic chest disease —middle-aged men with respiratory symptoms—to-day offers particular opportunities for this application of the epidemiological method.

TABLE III.—*Coronary and Cerebrovascular Disease Among Medical Practitioners.*[20 29] *Number of "First Attacks,"* 1947–50 (*Men Aged* 40–64)

	General Practitioners	Other Doctors
Coronary heart disease	82	33
Cerebrovascular disease	14	13
Man-years of observation	10,800	8,620

(The reverse is also true—that the epidemiological method may help to show or to confirm that apparently disparate phenomena are connected, by drawing attention to their related behaviour in the population—for example, malformation and rubella,[12] rheumatic fever and streptococcal infection, zoster and chicken-pox. However, I cannot think of any satisfactory illustrations from the non-infectious diseases.)

VII. Clues to Causes

The main function of epidemiology is to discover groups in the population with high rates of disease, and with low, so that causes of disease and of freedom from disease can be postulated. The most obvious and direct examples are the original observations on the nutritional deficiencies (scurvy, beriberi, pellagra, goitre); the geographical study of cancer (especially of the skin and liver); the industrial cancers (bladder, for instance); and industrial accidents (of coal-miners or railway workers). The biggest promise of this method lies in relating diseases to the *ways of living* of different groups, and by doing so to unravel "causes" of disease about which it is possible to do something.

"Ways of living" can usually be described only in simple terms, and the kinds of causes of health and disease postulated in them tend therefore to be in rather simple terms, not of intimate biological mechanisms, but of social factors in the satisfaction of elementary human needs, of large-scale environmental features, of major aspects of behaviour. They are thus often "general" rather than specific factors of health, causes of *dis*-ease, or diseases, rather than of a particular disease: as in the relations of water supply to bowel infections (not merely the cholera), living space and respiratory infections (as a class), income levels, nutrition and growth. We are only just beginning to identify such factors in ways of life, mass habits and social customs which may be related to many of the important problems of our own highly advanced society. For example, *overnutrition* (obesity; and ? atherosclerosis, thrombosis, dental caries, diabetes, toxaemia of pregnancy); *physical inactivity* (? "coronary thrombosis" and ? how much else); *tobacco and smoking* (oral and lung cancer—a "specific," rather, this—"coronary thrombosis"; and ? how much else); *atmospheric pollution* (lung cancer; ? chronic chest disease of many kinds, and ? acute, and ? other, non-respiratory conditions); *cultural factors* (genital cancer in Jews and non-Jews); *eating customs* (? alimentary cancer); "*social isolation* (? schizophrenia, senile psychosis, suicide). And, of course, there is still an overabundant heritage of nineteenth-century (and earlier) *poverty* and *crowding, insanitation* and *bad habits* that contribute over-fully to modern ill-health.

Fig. 7 illustrates from some recent studies, and includes a wide range of data, from the first turning of the ground to highly advanced observations. I have included (B) the famous analysis from the "Metropolitan Life" on the dangers of "overweight"; an elaboration of Doll and Bradford Hill's classic data on cigarette-smoking and cancer of the lung (E); some figures (unique so far as I know) from France on consanguineous marriages in relation to stillbirth and early neonatal mortality (G); an example (H) of the recent pioneering by the General Register Officer in psychosis, the darkest area of all; figures from Revans on the size of industrial units in relation to the frequency of accidents (D), which raise large questions of morale and the human environment, of *group* functioning as such, rather than the properties of the *individuals* who aggregate the group (compare immunity, and endemicity of infections). The distributions shown (A) on physical activity (they are different for *gastric* ulcer, incidentally, and for diabetes in *younger* persons, and do not show with other diseases), and on the disadvantages of town dwellers in respect of respiratory disease (C), merely set a stage for further inquiry; the natural experiment, or "experiment of opportunity" provided by miners and clerks (F), provides, at least, contrast groups in which it may be profitable to seek factors that are significant in modern infant mortality.

The great advantage of this kind of approach to prevention is that it may be applicable in the early stages of our knowledge of diseases, to disrupt the pattern of causation before the intimate nature of diseases is understood. Sufficient facts may be established for this by epidemiological methods alone, or in combination with others. The opportunity may thus offer to deal with one "cause," or with various combinations of causes. Moreover, the possibility of two types of control may be opened up—environmental (as in the fluoridation of water) and personal (through alteration of diet and hygiene).

Conclusion

Epidemiology is to-day the Cinderella of the medical sciences. The proposition might, however, be advanced that public health needs more epidemiology, and so does medicine as a whole, and, it may be said, society at large. *Public health* needs more epidemiology—this is the most obvious intellectual basis for its further advance. Epidemiology, moreover, as a tried instrument of research—with its modern developments in sampling and surveys, small-number statistics, the follow-up of cohorts, international comparisons, field experiment, and family study; and with its extensions to problems of genetics as well as environment, to physiological norms as well as disease, the psychological as well as the physical, morbidity as well as mortality—epidemiology now offers the possibility of a new era of collaboration between public health workers and clinical medicine. Such a collaboration could be on equal terms, each making their particular contribution to the joint solving of problems. There is abundant evidence to-day that clinicians would very much welcome such a development.

Medicine as a whole needs more epidemiology, for without it cardinal areas have to be excluded from the consideration of human health and sickness. Epidemiology, moreover, is rich with suggestions for clinical and laboratory study, and it offers many possibilities for testing hypotheses emerging from these. One of the most urgent *social* needs of the day is to identify rules of healthy living that might do for us what Snow and others did for the Victorians, and help to reduce the burden of illness in middle and old age which is so characteristic a feature of our society. There is no indication whatever that the experimental sciences alone will be able to produce the necessary guidance. Collaboration between clinician, laboratory scientist, and epidemiologist might be more successful. The possibilities are at present unlimited, if often neglected.

Summary

We may summarize what has been said in terms of some of the relations between epidemiology, and the epidemiological method, and clinical medicine.

Epidemiology studies populations, and all cases that can be defined in them. It is concerned not only with those whose troubles immediately present to particular clinical attention but with the subclinical, the undiagnosed, the cases treated elsewhere. It thus *helps to complete the clinical picture* and natural history of disease.

Epidemiology *supplements the clinical picture*: by asking questions that cannot be asked in clinical study—about the health of the community and of sections of it,

Figs. 7A–H.—Seeking Clues to Causes

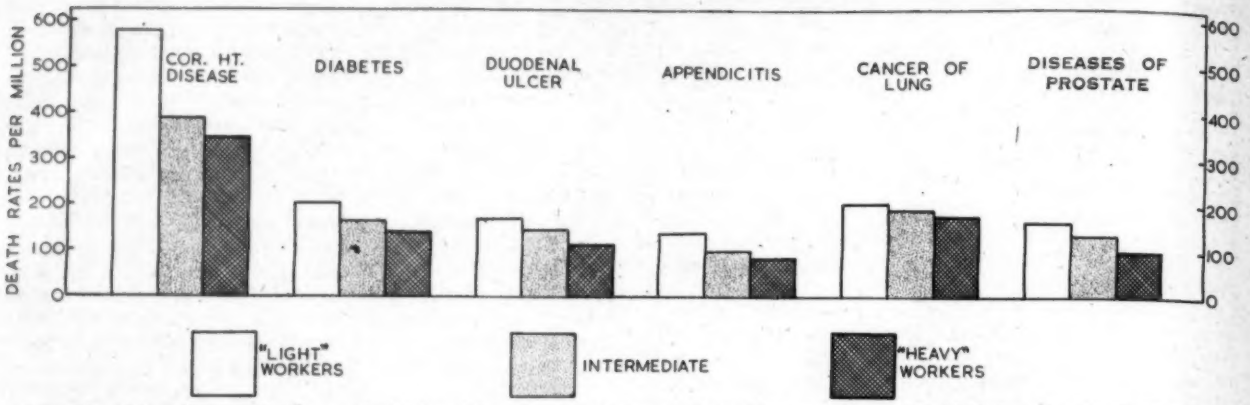

FIG. 7A.—Mortality in relation to physical activity of work. Men aged 45–64 in social class III (skilled workers). England and Wales. 1930–2.[18 28]

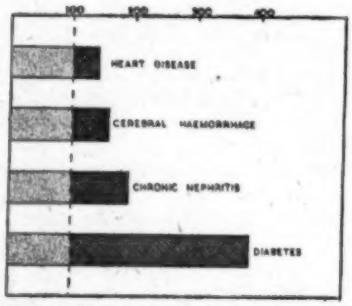

FIG. 7B.—Experiences of overweight men in comparison with standard policy holders. Metropolitan Life Assurance Company.[9] Actual number of deaths per 100 of expected. Ages attained 25–74.

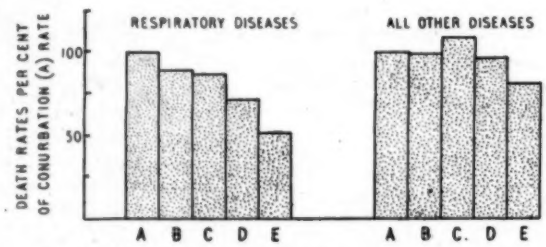

FIG. 7C.—Mortality of town and country dwellers from bronchitis, pneumonia, respiratory tuberculosis, lung cancer; and from all other diseases (males). Aged 45–64. England and Wales. 1950–2.[21 28] A=Conurbations. B, C, and D=Large, medium, and small urban areas. E=Rural areas. (The trend for females is very similar.)

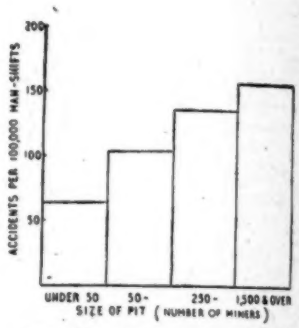

FIG. 7D.—Frequency of accidents and size of pits.[1]

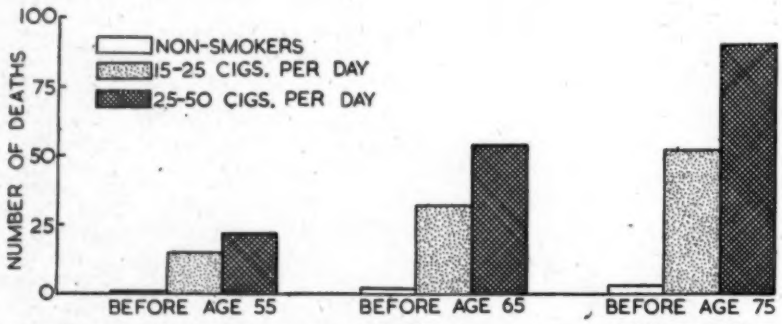

FIG. 7E.—Smoking and lung cancer.[8 11] Number of men per 1,000 aged 25 expected to die from cancer of lung before ages shown.

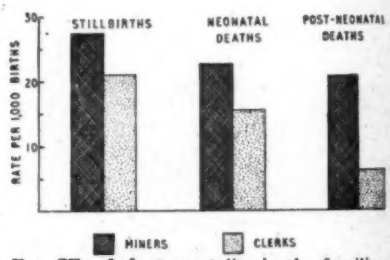

FIG. 7F.—Infant mortality in the families of miners and clerks. England and Wales. 1949–50.[19]

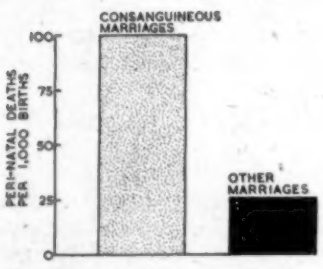

FIG. 7G.—Stillbirths and deaths in the first four weeks of life. Infants of consanguineous and other marriages. Two French *départements*.[20]

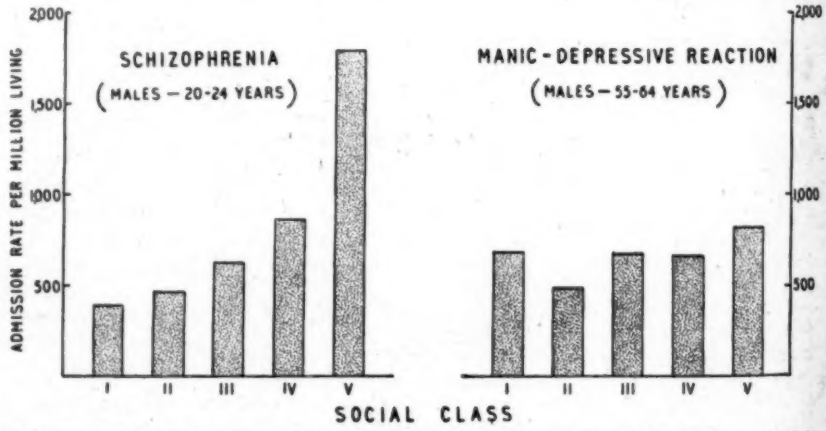

FIG. 7H.—Social class and admissions to mental hospitals. England and Wales. 1949.[24]

present and past; by setting clinical problems in community perspective, describing their behaviour as group, not individual, phenomena, indicating their dimensions and distributions, and how much, and where, action is needed; by revealing problems and indicating where among the population these might best be studied.

Finally, epidemiology by identifying harmful ways of living, and by pointing the road to healthier ways, *helps to abolish the clinical picture.* This is its chief function and the one in greatest need of development to-day.

I am grateful to my colleagues outside and in the Unit for much help; and in particular wish to thank Mr. C. Daly and Mrs. V. P. Hall for help with the figures.

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A remarkable expansion of work for the blind in the Colonies has taken place in the five years since the British Empire Society for the Blind was formed. The Society's fifth report can claim that in territories which contain more than two-thirds of the colonial population "the number of blind children at school has doubled; the number of blind adults in training has increased tenfold. Thirty new schools and training centres have been established, six more are being built, and an additional 18 have been planned. Braille alphabets have been devised for practically every written language in the Colonies." In West Africa, where the blindness rate is 20 times higher than in the United Kingdom, an ophthalmic team directed by Dr. F. C. Rodger is investigating the causes of blindness; an entomological team directed by Dr. G. Crisp is investigating the *Simulium* fly, whose bite causes "river blindness" (ocular onchocerciasis), and seeking a local means of controlling the pest. £20,000 was raised for the British West Indian blind. Half the blindness in the Caribbean territories "could be prevented or cured if more eye specialists were available and if people took better care of their eyes." The Society hopes to raise £20,000 of new revenue in the coming year.

ASSESSMENT OF ADRENOCORTICAL FUNCTION IN CASES OF PITUITARY TUMOUR*

BY

H. J. CROW, M.A., M.B., Ch.B.

Formerly Senior Resident Medical Officer, Frenchay Hospital, and Clinical Assistant (Research) to the Bristol Neurosurgical Unit and Bristol Royal Infirmary

This study concerns the assessment of adrenocortical activity in 18 cases of pituitary tumour. The application of the results to the surgical management is described.

The hazard of operation in some cases of adenoma or cyst of the pituitary gland is well known. Jefferson (1940) pointed out that "intracranial extension" of the tumour greatly increases operative mortality. In recent years there has developed an increasing awareness of the part played by pituitary insufficiency in post-operative death in these cases (Henderson, 1939; Grant, 1948; Bakay, 1950; Caughey *et al.*, 1952; Caughey and Garrod, 1954).

It was felt that in the complex polyglandular failure associated with pituitary tumour it might well be the adrenocortical deficiency which was dangerous to life at the time of operation. The hypothesis, then, which stimulated this study was that in cases of pituitary tumour operation might precipitate death in acute or subacute adrenocortical failure, and that corticotrophin (A.C.T.H.) might restore adrenal function and prevent death.

The object of this investigation was to produce a practical plan of management which could be followed routinely in the unit, excluding tests involving complex or time-consuming analyses. The selected tests, which are discussed below, were the glucose-tolerance test, the diuresis test of Robinson *et al.* (1941), and the fractional test meal.

Observations and Results

This series of 18 cases consists of all the patients admitted to this unit between 1951 and 1953 for operation on a pituitary tumour. Sixteen had an adenoma and two had a cystic craniopharyngioma. The indication for surgery was progressive visual loss in all cases. With one exception lesions were all exposed by transfrontal craniotomy.

The presentation of the observations on which this paper is based has posed a problem. A system of allocation of points has been chosen, arranged so that a score of 10 represents normality.

The scoring has been made out for each case on clinical estimation and on the results of the biochemical tests. In the clinical scoring points were added to or deducted from the normal rating of 10. The following features were considered as evidence of pituitary–adrenal hyperactivity: "moonface," hirsuties, and the type of obesity seen in Cushing's syndrome. Points were deducted for loss of energy, susceptibility to cold, impotence, testicular atrophy, Fröhlich type of obesity, loss of secondary sexual hair, infrequency of shaving, and soft finely wrinkled skin. Obviously there can be no precision in translating a matter of clinical judgment into numerical symbols, but the method has seemed practical enough for the purpose.

In the test-scorings the following data were used. Only the points for the sugar curve and the diuresis test were

*Based on a preliminary report read to the Society of British Neurological Surgeons at Zurich, June, 1952.

employed in the assessment, each being given 5 points for a normal result. The test-meal scores have been included for comparison only.

TABLE I.—*System of Scoring*

Score	Sugar Curve: Peak Value (mg./100 ml. Blood)	Diuresis Coefficient "A"	Test Meal: Peak of Acid Curve (ml. N/10 HCl/100 ml. Gastric Contents)
5	180–135	25 and over	30 and over
4	135–125	25–18	30–20
3	125–115	18–10	20–10
2	115–100	Below 10	Below 10
1	Below 100		
6	180–250		
7	Above 250		

Comparison of Clinical and Test Scorings (See Table II)

In 15 cases there was either clinical or test evidence of increased or reduced activity of the pituitary gland. In only 8 of these was there a similarity in the clinical and test assessments. In three cases (Nos. 1, 4, and 7) the tests fell short of normal, but the clinical state was normal or near normal. In two cases (Nos. 8 and 13) the test scores were nearly normal, although clinically these patients showed a considerable degree of hypopituitarism. Again (Case 16), a woman with signs of hypercorticism, including "moonface," hirsuties, and hypertension, had a high blood sugar curve (peak 210 mg. per 100 ml.—test score 6), but a low diuresis coefficient "A" (9.9—test score 2). One woman (Case 17) with middle-aged obesity appeared normal, yet her high sugar curve began at 138 and reached a peak of 280 mg. per 100 ml. In the absence of clinical evidence of diabetes mellitus, these high sugar curves were interpreted as signs of increased pituitary–adrenocortical activity. This interpretation is supported by post-operative observations in Case 16, where, after partial removal of her pituitary tumour, the blood glucose peak fell from 210 to 145 mg. per 100 ml. Her plethora and hypertension also decreased. However, this evidence is not conclusive.

Of the 11 men, four (36%) were impotent, a proportion which agrees with the observations of Bakay (1950). The four impotent men (Cases 2, 3, 8, 13) all showed marked clinical evidence of pituitary insufficiency, but Cases 8 and 13 had normal or near normal adrenocortical function as judged by the tests. The clinical scoring in Case 4 (aged 56) was normal; he was potent and had a family of six, yet his total test score was only 7. Impotence was the rule if there was more than slight clinical evidence of pituitary insufficiency. It seems, therefore, that neither sexual potency nor the general clinical picture is necessarily reflected in the level of adrenocortical activity as revealed by these tests.

Neither the clinical state nor the test results bore any relation to the size of the tumours. There were no basophil or pure eosinophil tumours in this series. A comparison of the clinical test findings with the histology of the tumours will be published later.

The case material is now considered in groups based on whether hormone therapy was given before or after operation, or not at all.

Group A: Pre-operative Hormone Therapy

One-third of the patients were considered to need pre-operative corticotrophin treatment. The selection in these six cases was generally easy. In Cases 3, 5, and 6 there was clinical and test evidence of adrenocortical deficiency, and the indication for the therapy was obvious. In Cases 1 and 4, in spite of a good clinical state, the test scores were only 8 and 7 respectively, and corticotrophin was prescribed. The patient in Case 2 had been given testosterone propionate for a month before admission to the unit, with considerable improvement.

Of the six cases four made smooth uneventful recoveries. One of these (Case 4) had a large globular "intracranial extension" (cf. Jefferson, 1940). Case 6, a slight undeveloped boy of 13 years, had total removal of a craniopharyngioma. This is a very hazardous procedure, but he gave no post-operative anxiety. Case 5 did not recover from the operation, and died next day: necropsy revealed a large intracerebral haemorrhage.

In Case 3 (a man of 41, with a severe degree of pituitary insufficiency) a low adrenocortical test score of 4 rose to normal after five days' treatment with corticotrophin. He felt more energetic than he had done for years, and in general his pre-operative state was satisfactory. His case has been described elsewhere (Houghton, 1953). The mistake made in this case was to stop the corticotrophin one week after operation, neglecting the fact that his pre-operative pituitary function was gravely impaired. On the ninth day the craniotomy was reopened because of suspicion of intracranial clot. None was found. That night he passed into a pituitary crisis. The blood chemistry was as follows: sodium 288 mg., chloride 540 mg., potassium 18.2 mg. per 100 ml.; and CO_2 combining power, 51 vols. per 100 ml. He was given 30 g. of sodium chloride in a short period, and large doses of corticotrophin (cortisone was not then available). He slowly recovered from the crisis, but during the next few weeks developed a severe extrapyramidal type of rigidity involving all muscle groups. This led to recurrent attacks of aspiration pneumonia, during one of which he died. Necropsy revealed softening of the anterior inferior part of the right putamen and internal capsule, and the white matter investing the lower border of the putamen. This was thought to have occurred during the prolonged hypotension of the pituitary crisis. The testes, and in particular the adrenals, were small.

The lessons to be learned from this case are: (1) in cases with severe pituitary insufficiency, supplementary hormone therapy should not be stopped after operation, but changed gradually into permanent replacement therapy; (2) progressive post-operative pituitary insufficiency may develop insidiously over a period of days, and a pituitary adrenal crisis may be precipitated by any added stress—for example, re-exploration of the craniotomy.

Group B: Post-operative Hormone Therapy

Case 7, a normal-looking athletic young man, presented with a subarachnoid haemorrhage from a pituitary tumour. On recovery from this bleeding his test score was only 6, but he came early in the series and no corticotrophin was available for him. He developed post-operative brain swelling and was returned to the theatre for decompression. During the following week he gradually sank into a state of torpor. By the seventh day he was immobile, incontinent, and only grunted on stimulation. Testosterone propionate, deoxycortone acetate (D.C.A.), and thyroid were started, and 24 hours later he was continent, speaking and eating. Thereafter he made steady progress. A month later he was weaned from the hormone therapy without distress.

Case 8 had a large irregular intracranial extension of his adenoma. He had fairly marked signs of pituitary insufficiency, but a normal adrenocortical test score. He was in a state of torpor throughout the first post-operative month. The tests were repeated and were found to have fallen significantly below normal. Testosterone, D.C.A., and thyroid were given, and thereafter he made slow but steady progress.

Case 9 was a stocky rather fat man, with no signs of hypopituitarism. His test score was 11. After operation he developed cerebral oedema, verified by reopening of the wound and treated by extension of the craniotomy. His condition deteriorated, and the indications of an approaching pituitary crisis were manifest. He was given corticotrophin, and thereafter made uninterrupted progress.

Group C: No Hormone Therapy

Six of the nine patients in this group had, by clinical and laboratory tests, at least average pituitary and adrenocortical function. Two (Cases 11 and 13) showed some signs of pituitary inadequacy, but their tests gave normal or near

normal results. One (Case 16) had considerable signs of hypercorticism, with a high glucose-tolerance curve but a low diuresis coefficient.

In six cases convalescence was excellent. Convalescence in Case 15 was delayed by persistent vomiting due to a hiatus hernia with oesophagitis.

Two patients died. In Case 10 there was a bleeding diathesis. The cause of death was post-operative clot. In Case 18, a boy of 5 years, a carotid artery was damaged during removal of a craniopharyngioma, and he died soon after operation in hypothalamic crisis.

Age and Sex Distribution

Comparing the men and women, three interesting points of difference are brought to light. (1) The ratio of men to women is 2:1. (2) The women fall within a small-scatter age group (46–54) at the period of the menopause. The men fall within a large scatter age group (26–56), most of them being within the years of sexual vigour. (3) All five women were in the period of declining ovarian activity, but in only one was there evidence of pituitary insufficiency. Eight of the eleven men, on the other hand, were aged 41 or under, but pituitary function was depressed in five. The literature corroborates the predominance of men in reported surgical series, with a ratio in the neighbourhood of 1.5:1.

An analysis of age grouping and endocrine state in both sexes has not been made in the large published series; but in this small series the women, on an average, presented for surgery ten years later than the men, and were less affected by pituitary insufficiency. If these facts are not chance findings in a small series they are difficult to explain.

The Tests

Glucose-Tolerance Test.—In cases with pituitary tumour there is a strong probability that a low flat type of curve is due to adrenocortical deficiency. A very wide range for "normality" has been allowed in scoring for the blood-glucose levels (Table I). As already stated, a high sugar curve, in the absence of the clinical syndrome of diabetes mellitus, has been interpreted as evidence of increased adrenocortical function. The results of the tests are given in Table II. In all the five patients who were given corticotrophin the curve rose significantly. In three the fasting blood-glucose level rose proportionately with the peak of the curve; but in two the fasting glucose level increased only by 4 and 5 mg. per 100 ml., whereas the peaks rose by 40 and 35 mg. per 100 ml. Another patient, in post-operative torpor, showed no change in the level of fasting blood sugar, but the peak sugar level had fallen

TABLE II

Case No.	Sex and Age	Clinical Estimation of Pituitary Function	Biochemical Estimation of Adrenocortical Function								Operation and Post-operative Course
			Before Corticotrophin				After Corticotrophin				
			G.T.T.	Co"A"	F.T.M.	Total or Adjusted Score	G.T.T.	Co"A"	F.T.M.	Total or Adjusted Score	
			Group A. Pre-operative Hormone Therapy								
1	M 26	10	5	3	5	8	5	5	5	10	Subtotal removal of small adenoma. Rapid and uneventful recovery
2	M 32	8	3	—	5	6	—	—	—	—	Transphenoidal decompression and aspiration of haemorrhage into adenoma. Rapid and uneventful recovery
3	M 41	5	1	3	4	4	5	5	5	10	Subtotal removal of moderate-sized cystic adenoma. Post-operative pituitary crisis after stopping corticotrophin. Died months later as result of crisis
4	M 56	10	2	5	3	7	5	5	5	10	Subtotal removal of large globular adenoma with "intracranial extension." Rapid and uneventful recovery
5	F 46	6	4	2	4	6	5	—	—	10	Aspiration and partial removal of small cystic adenoma. Died soon after operation from large intracerebral haemorrhage
6	M 13	6	3	3	2	6	5	5	4	10	Total removal of small (1 in.—2.5 cm.) cystic craniopharyngioma. Slow but uneventful recovery
			Group B. Post-operative Hormone Therapy								
7	M 35	10	4	2	5	6	—	—	—	—	Craniotomy. Adenoma entirely intrasellar. Pituitary torpor. Rapid recovery with testosterone, D.C.A., and thyroid
8	M 53	7	5	5	5	10	—	—	—	—	Partial removal of large adenoma with "intracranial extension." Pituitary torpor. Slow steady recovery with testosterone, D.C.A., and thyroid
9	M 37	10	6	5	5	11	—	—	—	—	Subtotal removal of very large globular adenoma Incipient pituitary crisis. Given corticotrophin. Thereafter uneventful recovery
			Group C. No Hormone Therapy								
10	M 40	10	—	5	—	10	—	—	—	—	Subtotal removal of small adenoma. Died soon after operation from large intracranial haemorrhage. Known bleeding diathesis
11	M 31	9	5	5	5	10	—	—	—	—	Partial removal of moderate-sized adenoma. Rapid and uneventful recovery
12	M 29	10	5	5	5	10	—	—	—	—	Subtotal removal of moderate-sized adenoma. Re-explored on sixth day. Rapid and uneventful recovery from both operations
13	M 51	7	5	4	5	9	—	—	—	—	Partial removal of large adenoma. Rapid and uneventful recovery
14	F 49	11	6	5	—	11	—	—	—	—	Aspiration and partial removal of large cystic adenoma. Rapid and uneventful recovery
15	F 48	10	6	—	5	11	—	—	—	—	Subtotal removal of moderate-sized adenoma. Convalescence delayed by persistent vomiting. Slow but good recovery
16	F 54	12	6	2	—	8	—	—	—	—	Subtotal removal of moderate-sized adenoma. Rapid and uneventful recovery
17	F 48	10	7	5	5	12	—	—	—	—	Subtotal removal of small adenoma. Rapid and uneventful recovery
18	M 5	10	5	5	5	10	—	—	—	—	Partial removal of small firmly adherent craniopharyngioma. Died soon after operation in hypothalamic crisis

G.T.T.=Glucose tolerance test. Co"A"=Diuresis coefficient. F.T.M.=Fractional test meal. A total score of 10 is normal. A score of 5 for each test is normal. Scores above or below these figures indicate function greater or less than normal. Only the G.T.T. and Co"A" have been used in arriving at the final or adjusted score. The F.T.M. results are included for comparison only.

by 40 mg. per 100 ml., when compared with the pre-operative level. These data emphasize the importance of not relying on isolated blood-sugar readings. In five cases (one male and four females) the peak sugar levels before operation and without corticotrophin were 190, 213, 219, 280, and 210 mg. per 100 ml. respectively. Three separate hourly specimens of urine were taken during all glucose-tolerance tests, and the glucose estimations were done in the laboratory. In only one instance (Case 14) was glycosuria found, and that only when the blood-glucose level had exceeded 200 mg. per 100 ml. This evidence of a raised renal threshold was unexpected.

Diuresis Test of Robinson et al. (1941).—The value of this test is well established. The results of the tests are shown in Table II. Five patients with low diuresis coefficients were given corticotrophin. Within four or five days the coefficients had returned to normal in four, and near normal in the fifth case. These findings are in agreement with those of Chalmers and Lewis (1951).

Fractional Test Meal.—In a review of the literature on hypopituitarism Sheehan and Summers (1949) state that of 21 test meals recorded only three were normal, the remainder showing relative or complete achlorhydria. Tuerkischer and Wertheimer (1944) found that in rats adrenocortical hormone was necessary for the production of gastric hydrochloric acid and pepsin. The results of the tests are shown in Table II. They run roughly in parallel with the results of the other tests, but give no additional help in assessing adrenocortical function. However, in all three cases with low acid curves, in which test meals were repeated, there was a significant rise in the acidity curves after four days on corticotrophin. The rises were 40, 100, and 150%. These figures suggest that the fractional test meal is a useful index of response to corticotrophin. They also help to explain the reports of haemorrhage from, and perforation of, "silent" peptic ulcers in patients on treatment with corticotrophin or cortisone.

The adrenalectomies which are being performed experimentally at present afford an excellent opportunity for closer investigation of the role of adrenocortical hormones in gastric secretion.

Management and Dosage

The decision to give or withhold pre-operative corticotrophin was based on consideration of the clinical picture and the test results. When pre-operative corticotrophin was thought necessary the dose used was 10 mg. six-hourly. When it was used to meet threats of post-operative crisis the dose was 40 mg. at once and 20 mg. four- or six-hourly. When to stop corticotrophin is a problem. One to two weeks after operation on full dosage is usually sufficient. When it is decided to stop corticotrophin, withdrawal is gradual over six days.

When the patient is likely to need hormone replacement therapy indefinitely it is started as the corticotrophin is withdrawn. Oral cortisone is probably the most effective and convenient drug for long-term use. In two cases (Nos. 3 and 8) the polyhormonal regime as advocated by Robertson and Kirkpatrick (1951) was effective.

In two cases (Nos. 7 and 8) when testosterone, D.C.A., and thyroid were given to counter pituitary torpor the results were good. The doses used were: testosterone propionate, 100 mg., and D.C.A., 5 mg., intramuscularly; and thyroid, increasing from ½ to 1 or 2 gr. (32 to 65 or 130 mg.) daily.

In this series there was no evidence that corticotrophin predisposed to infection or delayed healing. In this connexion it is well to comment on the necessity of excluding pulmonary tuberculosis before giving corticotrophin.

Post-operative Syndrome

The literature contains only a few descriptions of the syndrome of pituitary insufficiency after operation on pituitary tumours, notably those of Caughey *et al.* (1952) and Caughey and Garrod (1954). The following account is compiled from the literature and from personal observation. The syndrome has been divided from pituitary torpor and pituitary crisis. These terms should be regarded only as labels of convenience.

Mode of Onset of Pituitary Torpor and Crisis.—The onset of the syndrome may occur in one of three ways. (1) The patient may recover from the operation incompletely and remain in torpor throughout the whole post-operative period. (2) Initial recovery may be satisfactory; but within a period of hours, or at most two or three days, the level of consciousness falls and the patient enters the torpid state. (3) Following added stress—for example, re-exploration for clot—the patient may within a few hours develop a pituitary crisis.

Pituitary Torpor.—In this the patient passes through the stages of drowsiness and stupor, and may eventually become comatose. The torpor may be halted spontaneously at any stage, or may persist for days or weeks until recovery or death ensues. In the early stages restlessness may be a feature, or from the start the patient may lie completely immobile, as if under the influence of an opiate, and perhaps with all limbs flexed. This can lead to intractable flexion deformities at the knees. The cause of this flexed attitude is not clear. The limbs resist passive extension, sometimes in the absence of any signs of an upper motor neurone lesion, arthritis, or myositis. To begin with, the patient answers questions slowly and obeys simple commands, but the amount of effort required to elicit a response increases. The quality and quantity of the response deteriorate until only a meaningless grunt is emitted.

Mental processes may remain lucid throughout, although grossly retarded, but confusion is common. Delusions and visual hallucinations occurred in one patient from whom a large adenoma with extension had been removed (Case 8). Before operation in this case mental changes had been noticed by relatives for a year or two (abstraction, slothfulness, and apathy). Querulousness amounting to negativism is not uncommon in the early stages, manifest as resistance to all routine nursing attentions. The querulous note of the voice and the childish whine are characteristic. Incontinence occurs in all but the milder cases of pituitary torpor, and its disappearance is an early sign of recovery. Vomiting may occur but is not usual.

During the stages so far described the blood pressure is normal or slightly low, but it is never low enough to account for the state of torpor or be in itself a threat to life. The pulse is normal or slightly fast, though it may be slowed when brain-swelling complicates the picture. The temperature is normal or slightly raised. Hypothermia has not been recorded.

Hypoglycaemia does not seem to be a marked feature of this state. Caughey *et al.* (1952) report four cases in which blood-sugar levels were within normal limits. In one of our patients in pituitary torpor (Case 8) a glucose-tolerance test gave a fasting blood-glucose value of 80 mg. per 100 ml. and a peak value of 105 mg. per 100 ml. From the scant information available to date the most that can be said is that the blood sugar may be normal or reduced, and that sugar tolerance may be increased. Severe hypoglycaemic levels have not been reported.

Serum sodium may be normal or reduced. Caughey and his colleagues report reduced levels in three of their four cases. Serum potassium is generally within normal limits, but may be a little raised. Caughey *et al.* noted a level of 21 mg. per 100 ml. in one of their four patients. In one of our cases the serum potassium was 22 and 27 mg. per 100 ml. on two occasions. A transient cardiac irregularity occurred in one case, in the form of an irregular sinus rhythm.

Recovery from torpor may occur spontaneously or may be effected by appropriate hormone replacement. Improvement usually proceeds slowly, but, other conditions being favourable, a complete recovery can be expected.

Pituitary Crisis.—This may occur as the terminal event in a prolonged pituitary torpor or develop rapidly after a short period of post-operative "decline." The signs of approaching crisis are a rapid deterioration in consciousness, passing into coma; a falling blood pressure which does not respond satisfactorily to intravenous infusions or cardiovascular stimulants; a rapid, thready pulse; and shallow slow respirations. The skin becomes cold, and a patchy pallor and cyanosis appear in the lips, cheeks, and extremities. These ominous signs advance rapidly and death occurs in a matter of hours.

The serum chemistry in one patient in pituitary crisis (Case 3) was as follows: sodium 288 mg., chloride 540 mg., and potassium 18.2 mg. per 100 ml.; the serum CO_2 combining power was 51 vols. per 100 ml. These figures support the hypothesis that such patients may die in acute or subacute adrenocortical failure.

Sheehan and Summers (1949) have fully described what they call "hypopituitary coma," occurring in cases of chronic hypopituitarism. There is a great similarity between the state they describe and the torpor and crisis of the surgical cases. Some points of difference—for example, degree of hypoglycaemia, temperature, and pulse rate—may be eliminated by further study.

It may be argued that the syndrome is due to frontal-lobe damage at operation, especially in view of the constancy of incontinence as a sign. The recovery of Case 7 from a week's progressive torpor and incontinence, twenty-four hours after instituting hormone therapy, suggests that frontal damage does not play a large part in the syndrome.

In short, it seems likely that the syndrome of post-operative pituitary torpor and crisis is the hypopituitary coma of Sheehan and Summers, modified by surgical trauma.

Summary

An investigation has been carried out into the part played by adrenocortical deficiency as a cause of death after operation in cases of pituitary adenoma and cyst.

A scheme for pre-operative assessment of adrenocortical activity is described; and some steps to improve the prospects of surgical treatment are outlined. Some of the wider implications of the reported observations are briefly discussed.

Two syndromes of post-operative pituitary insufficiency are described, for which the terms "pituitary torpor" and "pituitary crisis" are used. Their relation to hypopituitary coma (Sheehan and Summers, 1949) is discussed.

From the results in the series described it seems permissible to infer that death from pituitary deficiency is largely preventable.

I am indebted to Mr. G. L. Alexander and Mr. D. G. Phillips for encouragement in this work and for facilitating these observations on their cases. Professor C. B. Perry, of the University of Bristol, helped materially in allocating supplies of corticotrophin furnished by the Medical Research Council. Mr. Yeoman and the staff of the hospital laboratory willingly undertook a multitude of investigations which were not initially of routine nature, and grateful acknowledgments are due to them.

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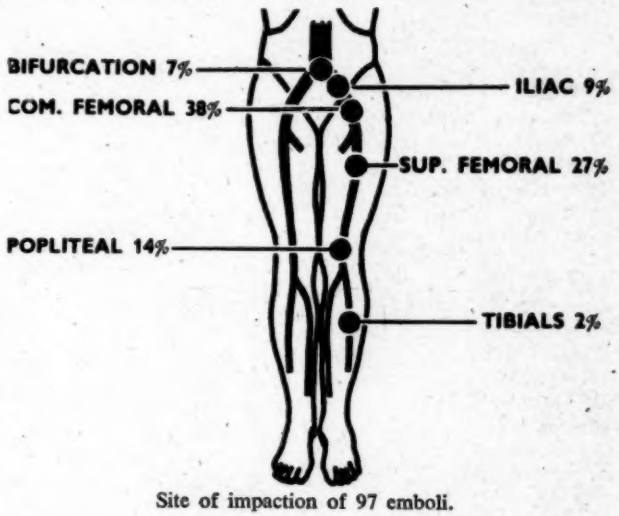
PERIPHERAL ARTERIAL EMBOLISM*

BY

R. P. JEPSON, M.B., B.Sc., F.R.C.S.

Professor of Surgery, University of Sheffield; Honorary Surgeon, Sheffield Royal Infirmary

The treatment of acute ischaemia subsequent to the impaction of a peripheral embolus has received considerable attention in the past quarter of a century, and during this period authoritative surgical opinion has spoken for and then against embolectomy. The extensive experience of Strömbeck (1935) and Key (1936) stimulated the publication of many reports favouring embolectomy in the American and English literature. Such enthusiasm was frequently based on a small number of successful cases, and when larger series were reviewed the mortality of embolectomy was often high and the morbidity considerable. More recently the non-operative management has been stressed (Haimovici, 1950), supplemented by the use of heparin, vasodilator drugs, and sympathetic-nerve interruption. In the present paper a series of cases of lower-limb emboli treated in the last seven years by the conservative regime are analysed. An attempt is made to discuss the diagnosis and physiopathology of embolism and define more accurately the indication for conservative management and for operative intervention.



Site of impaction of 97 emboli.

TABLE I.—*Site of Embolism*

Heart		72 cases (100%)
Associated with fibrillation	84%	
,, ,, recent cardiac infarct	16%	

TABLE II.—*Sex and Age Incidence Among 72 Patients*

	20–29	30–39	40–49	50–59	60–69	70–79	Total
Males	1	1	6	9	6	2	25
Females	3	6	7	14	13	4	47

Details of Cases

Although the first embolectomy performed in this country was on the brachial artery (Jefferson, 1925), emboli in the upper extremity do not often constitute a surgical problem, and such cases will not be considered, attention being solely directed to 72 patients in whom 97 lower limbs were endangered by embolic occlusion. The site of the impaction of the emboli is shown in the accompanying diagram. This distribution follows that previously reported by Warren and Linton (1948) and Haimovici (1950). The origin of the

*A lecture delivered at the Royal College of Surgeons on October 12, 1954.

emboli was in the heart in every case, and in 84% was associated with a controlled or uncontrolled auricular fibrillation; 16% of the patients had recently suffered a cardiac infarct and mural thrombosis (Table I). The sex and age incidence is illustrated in Table II. As in previously reported series, the majority of the patients were over 40 years of age.

Clinical Course

Although it is well recognized that an embolic occlusion of a major limb artery can occur painlessly (Haimovici, 1950), the vast majority (95%) of the present series complained of pain at or shortly after the onset of symptoms. The patient on clinical examination was often too distressed to be a satisfactory witness, and any detailed analysis of the type of pain is partially vitiated by this fact alone. The site of the pain occasionally corresponded with the position of the impacted embolism, as described by Rykert and Graham (1938). Thus the first symptom of an aortic embolism was ache in the back and suprapubic region, and in the case of a femoral embolism was initially felt in the groin, the artery being non-pulsatile and tender when palpated within six hours of the onset of symptoms. More commonly the reference of pain was in the periphery of the limb, and was usually described as a sudden ache, cramp, or tight band, a description characteristic of the deep pain which follows muscle ischaemia. Such patients had usually exercised the leg at or shortly before the onset of pain. The fact that the pain was referred to a non-muscular area such as the dorsum of the foot does not necessarily mean its origin was not in muscle.

The experiments of Boyd *et al.* (1949) clarified the mechanism of such reference patterns. Patients with emboli in the proximal large arteries frequently complained of disagreeable paraesthesiae beginning in the toes and spreading proximally up the limb as the initial symptom, although these were often replaced or overshadowed later in the course by pain. The onset of symptoms is not, of course, coincident with the time of arterial impaction, but follows at an interval. The arguments in support of this and also of the muscular origin of the pain are well documented by Lewis (1936). In addition to pain frequent early symptoms were numbness, coldness, weakness or paralysis of the foot or leg; and in many cases a partial or complete paralysis of knee and foot movements came on within a few minutes of the onset of symptoms. Emboli lodging at the aortic bifurcation occasionally produced the desire to defaecate or pass urine, and haematuria or spinal cord involvement developed if the thrombosis spread proximally to include the renal arteries.

On examination the signs of acute ischaemia were present. The skin was initially cold and pale, later becoming cyanosed and mottled, recovery being associated with the pink flush of a reactive hyperaemia and gangrene with brown and blackish tints. The veins were collapsed peripherally, and the sensory loss, most marked to light touch and pinprick, spread centripetally up the limb, being greatest in the foot. The level of the changed sensation depended particularly on the site of the arterial occlusion, being approximately to the mid-thigh in aortic lesions, to the knee in common femoral, and to above the ankle in blocks of the superficial femoral or popliteal artery. Deep pain sensation disappeared last of all, and marked calf tenderness (or a positive Homan sign) was often present in an otherwise anaesthetic limb. Muscle weakness may be selective to single groups, but the most profound weakness was seen in the most distal muscles.

Immediately following the occlusion the involved muscle was flaccid, but within a few hours became swollen and firm, with an associated plantar deformity, and the patient greatly resented correction of this by splintage. Pulses distal to the occlusion were absent and oscillometric readings zero. With major emboli, such as those at the aortic bifurcation or with the sudden deterioration of the circulatory efficiency as in a recent cardiac infarct, the blood pressure often fell precipitately, a factor which must greatly reduce the collateral arterial circulation. Multiple or visceral emboli often complicated the clinical picture. Haimovici has previously drawn attention to the frequency with which a venous thrombosis develops in the ischaemic leg owing to the stagnant flow and the damage to the endothelial wall, a complication which further endangers the viability of the limb.

Differential Diagnosis

Unless an embolus is demonstrated at necropsy or operation the diagnosis is always presumptive. There are four conditions which can simulate with convincing detail a major arterial embolism.

(*a*) A thrombophlebitis in the deep leg veins may on occasion be associated with extreme reflex arterial spasm and has been described as phlegmasia caerulea dolens. In such limbs intense pain, marked cyanosis, paralysis, and sensory change may be observed, and the major pulses are impalpable. The swelling of the limb is, however, greater than that seen in the early stages of an arterial embolism, and the arterial spasm usually relaxes after a sympathetic-nerve block or heavy sedation. Toe or more massive gangrene can, however, develop with purely venous lesions.

(*b*) Thrombosis in the femoral or popliteal arteries is much more frequent than impaction of an embolism at that site, and, by reason of the acute ischaemia which it causes, may present a similar clinical picture. Indeed, examination of the affected limb may not permit a differential diagnosis to be made. Often the clinical history will bring out symptoms of a long-standing chronic ischaemia, such as cold feet or intermittent claudication, and examination of the patient will reveal other evidence of obliterative vascular disease. The absence of a cardiac lesion, such as a recent infarct or auricular fibrillation, is strong evidence in support of a primary thrombosis. Most commonly an acute thrombosis comes on in an artery which is already diffusely narrowed and a collateral circulation is already established. The final acute thrombosis does not, therefore, present such a complete ischaemia, and severe pain and gross sensory or motor loss are usually absent. The age of the patient is not of great value, as most emboli and most thromboses develop in patients over 40 years of age. When the diagnosis is doubtful it is preferable to treat the patient for a thrombotic lesion and avoid surgery.

(*c*) A dissecting aneurysm of the abdominal aorta may occlude the distal part of the vessel, and the patient presents with acute ischaemia of both limbs. The absence of a source of emboli may be the only differential diagnostic criterion.

(*d*) *Pseudo-embolism.*—Occasional cases present the classical picture of a major artery embolism with absent major pulses and the clinical sequelae of acute ischaemia. Within a few days all the peripheral pulses have returned with normal pulse pressure and the leg has completely recovered. Atlas (1942) believes that reflex spasm of the large proximal arteries provoked by a small peripheral embolism may be the explanation, while possibly in some cases the embolism is ground to pieces by the repeated blows of the pulse wave. In some instances the further migration of an embolism to a minor vessel may reopen a major artery. Cases of pseudo-embolism are rare and deserve detailed investigation.

Physiopathology

After its initial arrest the embolic mass is subjected to the repeated blows of the pulse wave, which may cause its further disintegration and migration. At the site of final impaction the artery is moderately distended, its wall reacting by oedema and cellular infiltration. The thrust of each pulse is transmitted through the embolism, and on palpation of the impacted artery may be mistaken for a normal pulse wave (Nordentoft's sign). Distal to the embolism the artery is collapsed and pulseless and its intraluminal pressure greatly reduced. The capacity of the collateral circulation may be such that within minutes the peripheral blood flow approximates to a normal resting level, although the distal pulse wave amplitude is decreased (Shepherd, 1950).

On many occasions the expected restoration of blood flow through collateral channels fails to occur, and many factors can be mentioned which may account for this. The patient with a severe cardiac lesion may have an insufficient blood pressure to force an adequate blood flow through the increased resistance incurred by the use of collateral vessels, or the embolism may lodge at a bifurcation site, such as the division of the common femoral artery, thereby obstructing the main vessel and its major collateral channel.

Some (Reynolds and Jirka, 1944; Holden, 1952; Nystrom, 1936) have described severe and persistent arterial spasm following the impaction of an embolism. This must be uncommon, and the decrease in arterial diameter distal to the occlusion is probably more often due to lowering of arterial pressure; for Burton (1952) has shown that, regarded physically, blood vessels are distensible tubes with a critical closing pressure. Secondary thrombosis is an inevitable sequel to embolic occlusion, and occurs maximally in the artery distal to the lodgment where the axial flow is slow and possibly turbulent. The rate of the thrombotic growth is inconstant, but after 12 hours is often of such an extent as to make its removal hazardous or impossible.

Principles of Conservative Treatment

The essentials of conservative treatment are to maintain blood pressure, relieve pain by heavy sedation, and relax the peripheral vasculature by body-heating. The limb itself should be maintained horizontal with the pressure points carefully protected at an environmental temperature of about 25° C. Although it is often recommended that temperatures below this should be used we have found it difficult, with such cooling, to ensure a satisfactory peripheral vasodilatation by body-heating. Vasodilator drugs are contraindicated because of their ineffectiveness even when injected intra-arterially (Catchpole and Jepson, 1954) and their hypotensive action may further imperil the patient or the limb. A paravertebral block, if adequately performed, may be of value in the differential diagnosis and in the treatment, particularly of the more peripheral emboli. It is difficult to see how a sympathetic block can significantly influence the collateral circulation at the root of the limb. Heparin is used if conservative management is decided upon but not when embolectomy is contemplated. It possibly has some value in restricting the spread of the secondary thrombosis.

TABLE III.—*Survival and Loss Rate in 97 Limbs After Embolic Occlusion*

	Limbs Affected by Emboli	Limbs Survived	Limbs Gangrenous
Aorta	7	3	4
Iliac	9	6	3
Common femoral	38	19	19
Superficial femoral	27	16	11
Popliteal	14	12	2
Tibial	2	2	•

Results of Conservative Treatment

Table III summarizes the rate of survival and loss due to gangrene of 97 lower limbs following embolic occlusion of a major artery. A common femoral embolism is arbitrarily defined as one in which it is possible to palpate the femoral pulse for not more than 2.5 cm. below Poupart's ligament. The decision to group an embolism as superficial femoral or popliteal was decided by oscillometry. It will be readily seen that 58 of the 97 limbs survived the acute ischaemic episode and 39 became gangrenous. If these cases are further subdivided into those with a proximal lodgment of the emboli (aortic bifurcation, iliac, or common femoral) and distal (superficial femoral, popliteal, or tibial), it is evident that the prognosis for limb survival is worse in the former. Table IV shows that 49% of the legs in the proximal group became gangrenous, in contrast to 30% of the distal. Although it is not easy to be certain of the exact location of emboli, the prognosis of those diagnosed as in the popliteal region is surprisingly good, and is comparable to Haimovici's (1950) 6.6% incidence of gangrene for emboli in a similar site. Overall patient mortality was 39% within a month of entry into hospital, and in the 22 patients who lost one or more limbs through gangrene the mortality from mid-thigh amputation was 41%, death usually occurring within a few days of operation (Table V). The 19 patients who did not require a mid-thigh amputation and who died within a month of entry into hospital succumbed to multiple visceral or cerebral emboli or cardiac failure.

TABLE IV.—*Incidence of Gangrene According to Site of Embolism*

Proximal group (aorta, iliac, common femoral)	49%
Distal group (superficial femoral, popliteal, tibial)	30%
Total incidence	40%

TABLE V.—*Outcome Within One Month of Admission to Hospital*

Survived	61%
Died without operation	26·5%
Died after mid-thigh amputation	12·5%

On follow-up of the patients who survived and were discharged home it is evident that the majority of the limbs suffered from a chronic ischaemia. Disagreeably cold extremities, ulceration, severe claudication, and rest pain were often seen in the months following discharge. Using conservative treatment, Warren and Linton (1948) found that 17 out of 24 lower limbs were lost in patients with emboli; and Haimovici (1950), after excluding cases of death shortly after admission, reported a collective incidence of gangrene of 34.9% for the lower extremities. Gangrene occurred in 65% of the common iliac and 55% of the aortic bifurcation emboli.

Discussion

As it is evident that the prognosis in patients with peripheral emboli varies according to the site of impaction, treatment may be appropriately considered on this basis. It has been well established that the results of conservative treatment when emboli occlude the aortic bifurcation or the common iliac artery are very poor (Warren and Linton, 1948; Haimovici, 1950; Andrus, 1950). Albright and Leonard (1950), in a collective review, reported 193 cases of saddle embolism at the bifurcation of the aorta. They found that 144 of these patients died owing to the direct complications of the impaction; amputation was performed in many of those whose life was spared. Although aortic embolectomy seems to be the most rational treatment, it is extremely difficult to assess the mortality of the operation because of the small number of cases reported and the natural unwillingness to publish disappointing results. The treatment which is adopted for aortic embolism cannot for that reason be based on statistics. It is, however, our present policy to advise aortic embolectomy as the treatment of choice.

Of the three approaches to the bifurcation of the aorta and the iliac vessels, the transperitoneal exposure under spinal or general anaesthesia through a left paramedian incision is the most satisfactory. The intestines are packed away and the aorta and its branches controlled with tape, clamps, or digital pressure. An incision is then made into one or both common iliac arteries and the clot rubbed down with finger pressure. Madden (1951) prefers a direct incision into the aorta. Temporary release of the clamps, first distal and then proximal, confirms the completeness of removal. The incisions are securely closed without any significant constriction to the artery by a single layer of interrupted or continuous sutures of No. 5 Deknatel. More distal clot may need an additional exposure of the femoral arteries. This, if required, should be performed while the iliac arteries are accessible so that any further clot can be pushed down through the femoral incision. When the embolus has been satisfactorily extruded the distal pedal pulses are immediately palpable. Failure to return means incomplete removal of the aortic or iliac clot or the presence of a separate more distal embolism. If thought necessary the lumbar sympathetic chains can be resected at the time of the abdominal exposure. Heparin is not given post-operatively as

the risk of thrombosis at the suture lines is held to be less than the risk of massive haematomata in the wounds.

Although the retrograde removal of an aortic embolism following the bilateral exposure of the femoral arteries has been advocated (Griffiths, 1938), it is extremely difficult in many cases to dislodge the clot from below, and the intimal trauma it involves readily leads to further thrombosis. Retroperitoneal exposure of the aorta is more difficult and has no particular advantage.

The results of conservative therapy in iliac or common femoral embolism where the femoral artery pulsation, when palpable, terminates within 2.5 cm. below the inguinal ligament are not impressive (Haimovici, 1950), many patients dying of the effects of limb gangrene or suffering the troublesome complications of chronic ischaemia. The exposure of this region is simple, and can, if necessary, be performed under local analgesia. Probably the number of patients saved by femoral embolectomy will not be great. Many will succumb, as under the non-operative regime, to the complications of the cardiac lesions or further embolisms. Strömbeck (1935) reported a 63% mortality following embolectomy in the lower extremities. The results, however, for limb survival are vastly improved and the sequelae of chronic ischaemia largely avoided.

Distal emboli in the leg or emboli involving the arm are probably most suitable for the conservative regime, as the dissection necessary to expose the smaller vessels destroys collateral vessels and closure of the incision severely narrows the arterial lumen.

The two limiting factors to embolectomy are the general condition of the patient and the time interval between the embolic impaction and operation. The former often excludes surgery, and the non-operative regime is perforce adopted. Although many embolectomies have been successfully reported where the interval is longer than 24 hours, the extension of the retrograde thrombosis is so rapid and soft-tissue necrosis so developed that operations beyond 12–16 hours are apt to be unsuccessful (Pearse, 1933). It is a sad reflection that only 20 out of the 72 patients reported in this series were admitted to hospital within 12 hours of the onset of symptoms. It is probable, therefore, that in any large group of peripheral emboli the majority of the patients will be most satisfactorily managed by non-operative regime. There are, however, some patients whose general condition permits the removal of emboli arrested at the common femoral and aortic sites. The eventual prognosis for such patients who are saved is not good. Strömbeck (1935) has shown that of 61 patients discharged from hospital after successful embolectomy one-half are dead from heart failure or further emboli within two years. Many surgical lesions, however, carry an equally grave prognosis, and by prompt intervention the surgeon can save many limbs and some lives and, as is his duty, relieve much suffering.

Many of the cases reported in this paper were seen in the Manchester Royal Infirmary, and I am grateful to Professor A. M. Boyd for stressing the importance of the conservative regime. Mr. W. Metcalfe has kindly allowed me to use some of his material, and the Department of Medical Illustrations provided the diagram.

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OCULAR NERVE PALSY WITH SEVERE HEADACHE IN DIABETICS

BY

W. P. U. JACKSON, M.D., M.R.C.P., D.C.H.

(From the Diabetic Clinic, Groote Schuur Hospital, and the Department of Medicine, University of Capetown, South Africa)

A diabetic patient presents with the complaints of double vision and of extremely severe headache behind the left eye and in the left frontal region. Examination reveals an isolated left-ocular-nerve palsy. No cause is found and the condition clears spontaneously. Is it a diabetic complication, pure and simple?

Isolated cranial-nerve palsies, especially of the third and sixth nerves, are known to occur in diabetics, either at the inception of the disease or later in its course.[1–12] That these palsies are in fact true instances of "diabetic neuritis" seems likely where no other cause can be found and where the paralysis is only temporary. According to Joslin and his group[7] the condition clears up as the diabetes is brought under good control, while Collier[1] reports total cure in all of his 30 cases.

Association of Ocular Palsy and Pain

We have seen several instances of diabetic cranial-nerve palsy in the past years, but have recently run into diagnostic difficulties over diabetic patients who present with severe headache in addition to their ocular palsies. Pain does not normally accompany such palsies; it is rarely mentioned in the literature. Groenouw[4] remarks upon the occasional association of "neuralgia of the fifth nerve" with diabetic ocular paresis, and Larson and Auchincloss[6] mention "numbness of the face" (presumably fifth nerve) without pain. Goodman *et al.*[3] report one case of "widespread neuropathy, including an attack of pain in the distribution of the right trigeminal nerve," and Herson[5] reports a case of internal and external ophthalmoplegia preceded by three weeks' bilateral frontal headache. Apart from these skimpy references all other authors either state that pain in head or face does not occur or else they are silent in this regard. In each of the present cases there was a strong suspicion of intracranial aneurysm (or similar localized lesion), but this could not be proved, and it was eventually believed that the syndrome was purely diabetic.

Case Reports

Case 1.—A coloured woman aged 48, known to have had diabetes for 18 months, not obese, and poorly controlled on around 30 units of zinc-protamine insulin daily, experienced very severe right hemicranial headache of sudden onset which was continuous and unrelieved by salicylates. There was no nausea, vomiting, or vertigo. The next morning her right eye was closed. Examination the same day revealed a complete right third- and sixth-nerve palsy and also hypoaesthesia to touch and pin, with mild paraesthesia in the distribution of the first division of the fifth nerve on the right side. She had no diabetic "complications" of vascular or other type; she neither drank nor smoked. Her past history and further examination were unrevealing. Radiographs and cerebrospinal fluid were normal; W.R. was negative in the blood and C.S.F. A right carotid angiogram was adequate and entirely normal. The headaches slowly abated; the neurological features were improving in three weeks, and had completely cleared within two months.

Case 2.—A coloured obese woman aged 50, with very mild diabetes of some nine months' duration (fasting blood sugar, 150 mg. per 100 ml.), who was controlled on diet only, suddenly developed an extremely severe right frontal

headache which spread to involve the hemicranium. This gradually improved over the next 14 days, but just when she felt quite well she became suddenly dizzy and saw double. She had a complete right sixth-nerve palsy. The past history and further examination were unhelpful. She "had never had a headache before." Her blood pressure was 150/110. Radiographs, C.S.F., and the W.R. were normal; permission to take an angiogram was refused. Improvement started after six weeks, and slowly the sixth nerve function became fully restored.

Case 3.—A coloured woman aged 50, of slim build, had had diabetes for four years. She was poorly controlled; in fact, she had omitted insulin for the past year, though actually needing some 30–45 units a day. She suddenly felt an intense right retro-orbital pain and right-sided headache, constant in nature and not relieved by ordinary analgesics. At the same time her vision became blurred, and the right eyelid closed two days later. We saw her after four weeks, when a partial right third- and fourth-nerve palsy was found with normal pupils and hypoalgesia in the area supplied by the first and second division of the fifth nerve. Nothing else transpired, except for the later appearance of angina pectoris of effort. Radiographs, C.S.F., and the W.R. were normal; a carotid angiogram was adequate and normal. The condition was actually improving when first seen (some four weeks from the onset), and restitution was complete in 10 weeks.

Case 4.—An undersized white boy aged 14, with severe poorly controlled diabetes of three years' duration, taking around 60 units of insulin daily with no definite diet, had had recurrent attacks of headache occurring above the left eye for two years, unaccompanied by nausea or vomiting. A complete left sixth-nerve palsy suddenly appeared, not definitely related to a bout of head pain. Other diabetic complications had already begun to appear, evidenced by retinal micro-aneurysms and sluggish tendon reflexes. Radiographs were normal; the W.R. was negative. Angiography was not performed. The paresis completely disappeared within three months, during which time no further headaches occurred.

Comment

It is admitted that in each of these patients, taken individually, the possibility of a non-diabetic local intracranial lesion has not been completely excluded. Even a normal angiogram does not afford total certainty in this regard. Taken together, however, I believe that these histories make a reasonable case for the existence of the syndrome of ocular palsy plus severe localized headache, caused by diabetes. I must admit that the fourth case is less convincing than the others. The combination of definite third- and fifth-nerve involvement in two cases suggests that it may be the latter lesion which produces the headache in the syndrome under discussion. Perhaps both nerves are involved by the "neuropathic process" where they run close together in the cavernous sinus.

It would appear that, as with other diabetic "complications," the severity of the diabetes bears no obvious relation to the emergence of this syndrome. In all cases it was temporary, although it might be argued that it cleared up as the diabetes was brought under better control.

Summary

Four cases are reported of severe localized headache with ocular-nerve palsies occurring in diabetic patients. In each case a "congenital" intracranial supraclinoid aneurysm (or similar local lesion) was suspected, but was not found, and the condition always disappeared within a few weeks. I believe it to be a variety of diabetic neuropathy, although I do not claim to have proved this.

I wish to thank Dr. S. Berman for allowing me to use the record of Case 1, which was under his care. I am indebted to Professors F. Forman, J. F. Brock, and G. C. Linder for their interest and advice.

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NEUROSIS IN GENERAL PRACTICE

BY

J. C. E. POUGHER, M.B., Ch.B.

Leamington Spa, Warwickshire

This paper forms an attempt to analyse the incidence, symptomatology, causes, and treatment of neurosis in a general practice. This practice is of medium size, consisting mainly of working-class patients in a town of 38,000 people.

Few papers dealing with the analysis of neurosis in general practice are available for reference, and nearly all are American. Klapman (1945), Bowman (1946), and Waggoner (1947) have written at length on the significance of psychoneurosis in general practice, and have estimated that it constitutes some 50% of the practitioner's work. Denker (1946) reviewed 500 cases of all types of neurosis treated by general practitioners; his paper is referred to later. O'Neill *et al.* (1954) however, made an analysis of "stress disorders" seen in three London area practices, and found that each day some 20% of patients seen were suffering from some type of neurosis, the figures for the rural practice being somewhat lower (10–15%). They emphasized the importance of diagnosing these patients in the practice and devoting enough time to treatment, and presented a number of examples.

Material

In order to avoid special selection, the first 500 consecutive patients from a given date (August 28, 1953), who sought consultation, whether at the surgery or in the home, were taken. Their names were entered in a book, together with their age and sex. Careful histories were taken, and all were examined thoroughly as soon as possible. A note was made if neurotic symptoms were present, and each case was regularly reviewed at intervals over the period of one year.

The 500 patients in the survey consisted of 273 females and 227 males. Evidence of neurosis was found in 50 (22%) males and in 131 (48%) females, making a total of 181 patients, or 36.2% of the whole. The ratio of 50 males to 131 females compares with Denker's analysis, in which he found a ratio of roughly 1:3.

An estimation carried out during the survey showed that in one month 47.6% of all consultations were sought by patients with some form of neurosis. Since many of these patients take up more time than those with physical illness it is clear that the neurosis is the biggest problem facing the general practitioner.

Table I shows the incidence of neurosis in these 500 cases. It will be seen that the greatest incidence of neurosis in

TABLE I.—*Incidence of Neurosis in Terms of Age and Sex*

Age Group	Neurosis			Other Cases			All Cases		
	M	F	Total	M	F	Total	M	F	Total
Under 30	7	27	34	52	53	105	59	80	139
30–40 ..	11	7	18	23	15	38	34	22	56
41–50 ..	7	22	29	23	16	39	30	38	68
51–60 ..	13	39	52	33	21	54	46	60	106
Over 60	12	36	48	46	37	83	58	73	131
Total..	50	131	181	177	142	319	227	273	500

both sexes is in the two oldest age groups—that is, 50% of the male neurotics and 57% of the female neurotics are over 50 years of age. It is interesting to note that the incidence of neurosis in the 41–50 group, in which the majority of menopausal women lie, is lower than in the 51–60 group. It will also be seen that women attending with symptoms of a neurosis exceed those attending with physical illness in all three older age groups. The average age of the neurotic patients was 49.6 years.

Symptomatology

All patients were given the opportunity of explaining their symptoms, and so far as was possible leading questions were avoided. When the neurotic patients realized that they were to get a sympathetic hearing there was little difficulty, in most cases, in getting a complete symptom picture. Each symptom was explored to determine its nature, distribution, intensity, and relation to function.

Altogether 172 symptoms were complained of by 50 males (3.4 per patient) and 512 symptoms by 131 females (3.9 per patient). An attempt to list these symptoms to indicate their relative frequency has been difficult and only partially successful (Table II). There was such variability in the nature of the symptoms that only a very wide classification was possible.

TABLE II.—*Incidence of Symptoms in Order of Frequency and Comparative Frequency in Both Sexes*

Symptoms (Male)	Incidence	Symptoms (Female)	Incidence
1 Abdominal pain ..	21	1 Headache	61
2 Depression	20	2 Depression ..	51
3 Headache	13	3 Tiredness ..	47
4 Tiredness	12	4 Abdominal pain ..	42
5 Chest pain	12	5 Insomnia ..	34
6 Flatulence	10	6 Vomiting ..	23
7 Irritability	9	7 Flatulence	23
8 Faintness	9	8 Miscellaneous pains and sensations ..	22
9 Insomnia	7	9 Dizziness ..	20
10 Breathlessness ..	6	10 Anorexia	19
11 Nervousness ..	5	11 Nervousness ..	18
12 Anorexia	5	12 Chest pain ..	16
13 Constipation ..	5	13 Faintness	15
14 Sensations in mouth..	5	14 Nausea	13
15 Dizziness	4	15 Back pain ..	12
16 Dysphagia	4	16 Diarrhoea ..	10
17 Loss of weight ..	4	17 Breathlessness ..	10
18 Vomiting	3	18 Menstrual anxieties	9
19 Back pain	3	19 Irritability ..	7
20 Excessive sweating ..	3	20 Sensations in mouth	7
21 Nausea	2	21 Palpitations ..	7
22 Diarrhoea	2	22 Urinary symptons	7
23 Pains in throat ..	2	23 Constipation ..	6
24 Palpitations ..	2	24 Dysphagia ..	5
25 Miscellaneous pains and sensations ..	2	25 Pruritus	5
26 Choking sensations	1	26 Loss of weight ..	5
27 Urinary symptoms ..	1	27 Pains in throat ..	4
		28 Choking sensations	4
		29 Excessive sweating	3
		30 Dyspareunia ..	3
		31 Rectal sensations..	2
		32 Loss of voice ..	2
Total	172	Total	512

"Headache" covered a wide range of head pains, of varying distribution and intensity, very often recognizable as of neurotic origin by the exaggerated method of description. The same applied to "abdominal pain" with its vague and wide distribution and the absence of physical signs. "Nervousness" also covered a wide field, including such symptoms as a tendency to jump at unexpected noises, dislike of the dark and of being alone, fear of traffic, etc.

The group "Miscellaneous pains and sensations" was classified as such by virtue of the bizarre and varied nature of the symptoms, impossible to put into any other group—for example, crawling sensations in the skin, twitchings, "cold water" sensations, various interesting and typical bone pains, etc. As can be seen from Table II, these symptoms are much commoner in the female.

Purely "nervous" symptoms—that is, headache, tiredness, insomnia, depression, dizziness, faintness, irritability, and nervousness—constitute easily the biggest groups of symptoms met with, accounting for 253 out of the 512 symptoms in the female (49%) and 79 out of the 172 symptoms in the male (46%). Gastro-intestinal symptoms accounted for 151 (29.3%) symptoms in the female, and 57 (33%) in the male. Thus, between them, these two groups accounted for 78.3% of symptoms in the female and 79% in the male.

It is worth noting the marked similarity in the incidence pattern in the two sexes.

The diagnosis of functional illness was suggested by the following points: (*a*) atypical nature of the symptoms, (*b*) the presence of anxiety or apprehension towards the symptoms or, as in hysteria, apparent indifference, (*c*) tendency to dramatize or exaggerate the symptoms, and (*d*) past history.

Causes and Precipitating Factors

It might be assumed that, at least in most cases, the emotional instability which is the basis of each neurosis has been established in early life. In studying these 181 cases it appears that they then fall into one of two groups: Group A, cases in which emotional adjustment has hitherto been largely satisfactory, only to break down under certain stress; and Group B, cases in which there appears to have been only partial adjustment since childhood against the stresses of everyday life.

Group A

The precipitating factors involved in these neuroses are listed in Table III. Here again there has been difficulty in classifying the factors, and some patients have been included in more than one factor group. There were 33 males and 94 females in Group A. Eight of the males and 44 of the females figured in two factor groups, and 11 females figured in three factor groups.

TABLE III.—*Factors Precipitating Neurosis (Group A)*

Precipitating Factors	Male	Female
1. Marital problems	5	38
2. Inability to cope with domestic stress ..	3	27
3. Fear of ill-health	6	17
4. Ill-health	14	4
5. Insecurity — Financial	—	6
5. Insecurity — Of old age	2	18
5. Insecurity — Other causes	—	8
6. Occupational stress	6	3
7. Lack of affection from children	—	5
8. " " " " parents	3	6
9. Jealousy of children	1	—
10. Responsibility for an invalid	—	10
11. Loss of a member of the family	1	8
12. Obesity	—	7
13. Deafness	—	4
14. Blindness	—	1
Total	41	160

Marital Problems.—This is the biggest factor group because of the large number of females included (38). This group has been confined to patients whose neurosis has been precipitated by disturbed relations with the husband or wife. In many cases inadequate sexual relations played a large part. It is clear that frank and honest instruction by parents on sexual matters, particularly to girls at puberty, would prevent much neurosis, especially in early marriage. The number of married women who were puzzled by the idea that sexual intercourse should be pleasurable was remarkable.

Case 142.—Mrs. T., aged 31, complained of headaches, fainting attacks, depression, and insomnia. The symptoms began soon after marriage five years previously and had gradually got worse.

She was never instructed about sexual relations by her parents, and the only reference to the subject occurred when she was 14, when her mother said, "Never let a man touch you." This was never amplified, and left her puzzled but, she claimed, unworried. She had never been friendly with men until she met her husband one year before marriage. He had had previous sexual experience (unknown to her) and persistently suggested intercourse. She was clearly horrified at the thought, but some five weeks before they married she consented. She was scared and ignorant, failed to have an orgasm, and was told by her fiancé that she was "abnormal." This worried her, and she was not helped by discovering that she was pregnant at the time of marriage. Her feelings consisted of guilt about her pre-marital intercourse, anxiety about her inability to have successful relations, and anger towards her husband for causing her pregnancy. Her pregnancy and confinement were uneventful, but sexual relations did not improve afterwards. Intercourse became less regular, her husband became more impatient, and made further remarks about her being "abnormal."

In some cases, although purely sexual relations appeared to be adequate, continued lack of affection by husband or wife eventually precipitated a neurosis.

Case 48.—Mrs. G., aged 59, complained of dysphagia, generalized abdominal pains, flatulence, pains in the rectum, dizziness, and headaches for many years. Physical examination revealed nothing of significance. On questioning she complained tearfully that her husband, although always giving her a generous housekeeping allowance, had never shown her any genuine affection after the first year of their marriage, although intercourse had been regular. Since then he had never once taken her out. He appeared to spend most evenings at his club, and resented inquiry into his activities.

Domestic Stress.—Here again the burden, as would be expected, falls on the females. In many cases there were a number of factors, or sometimes trains of events, precipitating the neuroses: cramped accommodation, poor cooking and toilet facilities, strained relations with other people living in the same house, "in-law" problems, nowhere to put baby outside, shortage of money, or hire-purchase worries, and many other everyday problems to which the susceptible individual may succumb.

Ill-health.—It is interesting to note that ill-health was the commonest factor in precipitating neurosis in the males (14 cases) and yet one of the rarest causes in the females (4 cases). It would seem that once physical illness is established in the female she is capable of better adjustment than the male. Perhaps this is because the male has a greater financial responsibility, fears the loss of his job, and particularly dislikes enforced inactivity.

Fear of Ill-health.—The incidence is proportionately equal in the two sexes (6 males, 17 females). Only patients who genuinely fear that they have serious illness and have developed a neurosis through this fear have been included in this group, and none that have merely sought consolation in ill-health.

In both this group and that in which neurosis has developed through actual ill-health there are a number of cases where the neurosis could have been prevented or cured by more judicious handling by medical advisers. A few careless words, a dogmatic statement without clinical basis, failure to examine thoroughly and reassure where only anxiety is present—these may not only allow a neurosis to take shape, they may cause it (Helsborg, 1950). Too often a patient is left in doubt about his illness and its possible outcome. In addition some consultants feel they are obliged to make a clinical diagnosis instead of giving a firm reassurance. However, general practitioners can help by giving the consultant some indication of the nature of the case, pointing out that, in the event of investigations proving negative, an uncompromising reassurance would be invaluable.

Case 111.—Mrs. F., aged 52, had a long history of functional symptoms, mainly headache, irritability, depression, and insomnia. She said that her previous doctor never examined her, but told her it was "all nerves" and that she must pull herself together. After two years, during which time she made no improvement, she was referred to a physician, who after examination and various investigations told her that he did not think there was anything wrong with her, but thought she might be mildly thyrotoxic. Two years later she was firmly convinced that she had thyrotoxicosis, despite taking a thiouracil preparation continuously during that time with no improvement in her symptoms. When it was suggested to her that she had not in fact got thyrotoxicosis, she said, "The specialist would not have mentioned it unless he thought I had, would he?"

Insecurity.—This problem, except in the elderly, seems to be decreasing in incidence, probably owing to fuller employment, a greater measure of independence among women, improved welfare services, and sickness benefit. However, when it occurs it may precipitate a neurosis which is difficult to treat.

Case 172.—Miss M., aged 51, complained of nerve pains in the abdomen and left side of her chest. They were stabbing in character, of an irregular and varied distribution, unaffected by meals, coughing, or exertion. She also complained of vomiting without warning, anorexia, and tiredness. Examination revealed no indication of physical illness. The symptoms had begun soon after her father died. She had nursed him for 30 years; her mother having died when she was only 20. Her two sisters had never taken their share of the responsibility and were very soon married. Her father had never allowed her to go to work, although their money steadily dwindled. When he died she was left with very little money, no training or experience of work, a feeling of loneliness, and fear of the future. She expected to be turned out of her house, and seemed to be getting no help or advice from her sisters. She had never had the opportunity of social intercourse, and was shy and timid and very conscious of her own inadequacy.

Group B

This group consisted of 17 males (34%) and 37 females (27%). These cases presented the most difficult problems in the series, since improvement lay in learning to adjust themselves not to a problem but to a way of life. All sought consolation in ill-health and all had done so since early adult life.

Many suffered predominantly from a sense of inferiority, often coupled with a feeling that they "were hard done by" (10 males, 9 females).

Case 145.—Miss R., aged 81, complained of "tearing headaches," vomiting attacks, tiredness, and anorexia. On examination she was thin but well preserved for her age, and, apart from a mild anaemia, showed no sign of physical illness. It was plain that there was a deep-seated dislike of her sister. She described how, as a child, she had always been considered by her parents as dull and unattractive, and was never as good as her sister at games or school work and, later, at housekeeping. Her parents died when she and her sister were in their twenties and they had lived together since. She had never been allowed to do the shopping or cooking, but only the menial jobs, and, generally, was treated as a child.

Others (6 males, 20 females) suffered predominantly from a lack of fulfilment.

Case 28.—Miss C., aged 44, had complained of fainting attacks, nervousness, generalized abdominal pain, flatulence, and vomiting unrelated to food for many years. She was a single woman of above average intelligence, and examination showed that she was physically well. She admitted that as a young woman her two great ambitions were to have a classical education and to get married and have children. Her parents never took her first ambition seriously, although they had sufficient money. As they grew old they expected her to keep house for them, were domineering, and gave her no freedom even when she became older. She had had no opportunity to meet the opposite sex. Of latter years she had begun to compose poetry, which she had printed at her own expense and sent to various magazines and even the Royal Household.

Of the remainder (1 male, 8 females), all that can be said is that they had almost totally inadequate personalities with a complete lack of ability to adjust themselves even to minor stress.

Treatment

In general practice the doctor is in the unique position of being able to institute some prophylaxis. Without interfering in domestic life, he can watch the emotional development of the children on his list and, where necessary, tactfully instruct parents, particularly in preventing their

children from becoming illness-conscious, in giving them a feeling of security and happiness, and an increasing measure of independence and opportunity to tackle problems for themselves. The need for early sex instruction has already been mentioned.

Prophylaxis is equally important in patients who show anxiety, and they should not leave the surgery without reassurance.

If a neurosis is suspected, a full history, both medical and emotional, should be taken, and a thorough physical examination made. If a neurosis is diagnosed, further investigation or reference to a hospital department should be avoided if at all possible, tempting though it may be, even at the risk of an occasional mistake. This is usually easier to retrieve than the mistake of fostering a neurosis.

Firm reassurance should be given and an attempt made to explain in simple terms how symptoms may be related to emotional stress and how this consolation in ill-health may occur. It is surprising how many patients are able to grasp the implications.

Placebos should not be given, since the patient will think, quite logically, that the giving of medicine or tablets indicates at least some element of physical illness. Where physical illness is present it should be explained that treatment is for this only. Sedatives, such as barbiturates, should be used sparingly and for only some of the more anxious patients, and never for those who show depression. No drug should be a substitute for the four basic principles—that is, full history, full examination, reassurance, and explanation. The history and examination are included because they are an inseparable part of the treatment.

Regular but controlled visits should follow, with discussion and explanation until it is seen that improvement is taking place. The intervals between consultations may then be lengthened and finally stopped.

Many may say that there is not enough time for these measures during a surgery session, but time spent at the first consultation will prevent the familiar weekly visits, with symptoms and self-pity, and demands for a variety of prescriptions, a formula which most general practitioners have come to loathe.

It is important that consultations should be controlled by the doctor and not the patient. Fortnightly visits are, in most cases sufficient initially, increasing to monthly intervals when definite improvement is observed. Less dependence on the doctor should then be suggested, and visits finally stopped when recovery appears to be complete.

Results of Treatment

Six patients left the district and could not be traced, three died, leaving 172 (123 females and 49 males) to follow up. Table IV shows the results after one year. These figures must be viewed with some reservation. "Apparent cure" has been so termed because additional stress on these patients may cause recurrence of symptoms. However, they are either symptom-free or only attending for treatment of purely physical illness. "Greatly improved" indicates that only occasional functional symptoms still exist. "Some improvement" indicates that these patients have over the year consistently complained of fewer symptoms, and admit improvement, but are still obviously suffering from a well-marked neurosis. "No change" indicates that either no progress has been made or relapse to the original state of the neurosis has occurred.

TABLE IV

Result	Males	Females	Total
Apparent cure	27 (55·1%)	65 (52·8%)	92 (53·5%)
Greatly improved ..	8 (16·3%)	28 (22·8%)	36 (20·9%)
Some improvement ..	6 (12·3%)	21 (17·1%)	27 (15·7%)
No change	8 (16·3%)	9 (7·3%)	17 (9·9%)
Total	49 (100%)	123 (100%)	172 (100%)

It will be seen that a little more than 50% were symptomless after one year in both sexes, and a total of 20.9% greatly improved. It is interesting that the figures are so similar in both sexes. Nearly 10% of patients show no change in their condition, the figure being more than twice as big in the males (16.3% compared with 7.3% in the females). However, the number of males in the survey is too small for anything to be deduced statistically.

Denker (1946) found that of 500 cases of neurosis treated by general practitioners in the U.S.A., 44.6 were apparently cured in one year and a further 27% in two years; 10% "remained disabled" after five years. He compared these figures with results obtained of patients treated in psychiatric centres in London, Berlin, and Chicago, and found them to be statistically very similar—that is, figures of 65% to 75% cured or greatly improved. This must be greatly encouraging to general practitioners genuinely interested in treating their neurotic patients.

Conclusions

The neurosis in general practice constitutes the biggest problem facing the doctor, taking up more than 50% of his time. These patients are as much in need of diagnosis and treatment as others, if not more so. Early diagnosis is vital, and for this a full history and examination is necessary. Much patience and sympathy is required, especially at the initial consultation, if the patient's confidence is to be gained.

It is a fallacy that patients will go elsewhere if they are not given medicine or tablets. Not one of the 172 patients in this series who have been reviewed for one year have sought alternative medical advice.

Specialist advice should be kept to a minimum in those cases where, for example, a chest *x*-ray or barium meal examination can be used to reinforce the practitioner's reassurance. It is certain that more help would be derived from consultants if they were informed that reassurance is what is required.

Finally, it is obvious that results can be, and are, better than expected if in the early stages enough time is devoted to gaining the confidence of the patient.

Summary

Of 500 consecutive patients seen in a general practice, 181 (36.2%) showed signs and symptoms of a neurosis; 131 were females and 50 were males.

In one month patients with neurosis constituted 47.6% of all consultations.

The age, incidence, symptomatology, and causes are discussed.

Methods of treatment are suggested and results are analysed.

I would like to thank Dr. J. M. Malins, of the General Hospital, Birmingham, for his helpful criticism and advice, and my wife for her patience and long hours of secretarial toil.

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A defence of isolation hospitals was made by Dr. HUGH MORRISON, Medical Officer of Health, Taunton, at a meeting of the Royal Sanitary Institute on July 21. He denied that they were largely obsolete. While he agreed that the isolation hospital should be closely integrated with the local general hospitals, he pointed out that the special nursing needed for infectious cases was best given by a staff "permanently engaged in this particular work."

INSULIN ZINC SUSPENSION IN CHILDHOOD DIABETES

BY

O. H. WOLFF, M.D., M.R.C.P., D.C.H.
Lecturer in Paediatrics and Child Health, University of Birmingham

AND

T. G. MADDISON, M.D., M.R.A.C.P.
Medical Registrar

(From the Children's Hospital, Birmingham)

In 1951 and 1952 Hallas-Møller and his colleagues described the composition and action of the new insulin zinc suspensions (I.Z.S.) produced by the Novo Laboratories in Copenhagen (Hallas-Møller, Petersen, and Schlichtkrull, 1951, 1952). Several reports have dealt with their use mainly in adults (Hallas-Møller, Jersild, Petersen, and Schlichtkrull, 1951, 1952; Lawrence and Oakley, 1953; Murray and Wilson, 1953; Oakley, 1953; Nabarro and Stowers, 1953; Stowers and Nabarro, 1953; FitzGerald *et al.*, 1954; Melton, 1954; Venning, 1954). Ferguson's (1954) study deals only with children.

Material

The present study deals entirely with I.Z.S. (insulin zinc suspension), which is a 3/7 mixture of I.Z.S. (amorphous)/I.Z.S. (crystalline). We started to use I.Z.S. in October, 1953, and have maintained 20 children on it for periods of from five to thirteen months. We have employed I.Z.S. in every new case (Cases 1–10) as well as in 10 patients (Cases 11–20) who had attended the diabetic clinic for periods of from two to seven years, and in whom the control achieved with either globin insulin (G.I) or a mixture of protamine zinc insulin (P.Z.I.) and soluble insulin (S.I.) was unsatisfactory. All cases were of the acute variety typical of juvenile diabetes.

Method

The 10 new and 8 old cases were admitted to hospital for stabilization on the new insulin. The remaining two (Cases 16 and 19) were changed to the new insulin as out-patients.

Diet.—The carbohydrate intake was measured. The amount of carbohydrate in the various meals is shown in the Table; one portion is equivalent to 10 g. of carbohydrate (Lawrence, 1952). Because the amount of dietary protein and fat varies little from day to day (Murray and Wilson, 1953), their intake was not measured.

Insulin.—I.Z.S. was given 20 to 30 minutes before breakfast. In the 10 new cases a rough estimate of the total insulin requirements was obtained during the first two or three days after admission by giving S.I. before the three main meals, the dose depending on the amount of sugar in the urine. On the third or fourth day the S.I. was replaced by a single dose of I.Z.S. In those children who had been under treatment with other insulins the previous dose was replaced abruptly by a single dose of I.Z.S.

Activity.—The nursing staff and occupational therapy staff ensured that the children admitted to hospital took an amount of exercise comparable to that taken at home.

Tests of Diabetic Control

In-Patients.—On an average it was not until three weeks had elapsed that urine passed before meals became sugar-free. At this stage, if the child had no hypoglycaemic attacks and was in good general condition, blood-sugar levels were studied over a 24-hour period. Capillary blood samples were usually taken at midnight, 4 a.m., 8 a.m., 10 a.m., midday, 2 p.m., 4 p.m., and 8 p.m., and the sugar content was estimated by the method of Rappaport and Pistiner (1934). In most cases the results suggested the need for only minor alterations in the diet or insulin dose—for example, in Case 1 (see Table) the insulin was reduced from 24 to 22 units, and the carbohydrate at tea-time was increased by 10 g. to a total of 40 g. It was not considered justifiable to subject these children to a second series of pricks. In a few cases, however, the diurnal blood-sugar curve was so grossly abnormal that it was repeated after the necessary changes in the insulin dose and/or diet.

Out-Patients.—To assess whether control was maintained after discharge the total amount of sugar in a 24-hour specimen of urine, collected in a Winchester bottle containing a small amount of toluene, was estimated. This test was carried out several weeks after discharge, and, when necessary, was repeated until good control had been re-established. The two children who were changed to the new insulin as out-patients had the 24-hour urinary sugar excretion determined when routine urine tests before breakfast and supper, isolated blood-sugar estimations, and freedom from hypoglycaemic attacks suggested that good control had been achieved.

By good control we mean that the child, while leading a normal life, is symptom-free and in good health, gains weight satisfactorily, and passes less than 10 g. of sugar in 24 hours. As the daily carbohydrate intake in every case was at least 200 g., this is equivalent to a sugar loss of less than 5%.

Details of Cases

Case No.	Age	Sex	As In-patient: Blood Sugar (mg./100 ml.)								I.Z.S. on Discharge from Hospital (Units)	As Out-patient: Present Carbohydrate Diet in Portions (1 Portion = 10 g.)					I.Z.S. Present Dosage (Units)	Urinary Sugar Excretion (g. in 24-hour Specimen)
			M.N.	4 a.m.	8 a.m.	10 a.m.	Noon	2 p.m.	4 p.m.	8 p.m.		Breakfast	Mid-morning	Dinner	Tea	Supper		
1	8	M	127	64	78	92	64	110	64	157	22	4	2	7	4	5	22	0·72
2	11	M	176	124	108	78	87	147	125	69	48	6	3	7	6	6	44	3·3
3	11	F	89	82	169	117	111	103	101	155	44	5	4	7	6	6	44	9·2
4	12	M	184	108	125	85	85	122	113	97	24	6	3	8	7	6	40	7·8
5	7	M	116	73	82	153	63	118	77	131	20	7	3	8	4	4	34	0·85
6	7	M	127	137	71	68	59	94	117	143	34	5	3	6	4	4	22	0·62
7	12	M	71	87	91	132	87	87	94	165	32	6	4	7	5	6	32	1·2
8	12	F	125	155	169	155	97	122	104	117	36	6	3	7	4	6	36	8·5
9	9	M	186	237	111	—	132	—	49	221	32	4	3	7	3	5	32	3·9
10	11	F	146	143	186	162	113	122	183	177	50	7	3	7	5	5	64	2·1
11	9	F	237	207	89	134	117	162	137	310	48	5	2	5	4	5	48	2·5
12	13	M	311	275	211	235	143	146	99	188	92	7	4	8	6	5	92	1·6
13	9	F	143	75	87	77	68	162	89	101	44	5	3	5	4	4	48	8·6
14	12	F	38	77	127	—	66	—	52	77	46	5	2	4	4	5	46	24·0
15	8	F	153	84	87	138	66	104	111	273	88	4	2	7	4	5	88	4·8
16	13	M	Changed as an out-patient								—	5	4	7	4	6	50	0·63
17	10	F	110	73	97	150	89	179	144	177	44	4	2	6	3	6	48	7·8
18	9	M	134	63	125	216	108	124	59	64	48	5	4	8	6	4	52	0·75
19	11	F	Changed as an out-patient								—	5	3	5	5	3	72	8·0
20	9	M	106	63	144	167	111	156	89	129	48	6	3	7	4	5	44	31·0

Results

The Table shows the results. In nine children, even though control had been achieved in hospital, the insulin dose had to be changed after discharge. In four (Cases 4, 5, 6, 10) the change exceeded 10 units. In a few cases minor alterations had also to be made in the carbohydrate content of the various meals. Ultimately good out-patient control was achieved in all but two children.

Case 14.—This patient was a 12-year-old girl who suffered from petit mal as well as diabetes mellitus. Before the change-over to I.Z.S. she had received a mixture of P.Z.I. and S.I., but it had been impossible, despite anti-convulsion therapy, to keep the urine sugar-free without precipitating numerous attacks of petit mal. This state of affairs remained unaltered with I.Z.S.

Case 20.—A 9-year-old boy, in whom a mixture of P.Z.I. and S.I. had not achieved satisfactory control, was admitted to hospital for restabilization on I.Z.S.; good control was achieved. His attendances at the diabetic clinic had not always been regular and a few weeks later he was readmitted in hypoglycaemic coma brought on by omitting tea and playing cricket. Response to intravenous glucose was immediate. Before discharge from hospital control had been re-established and a 24-hour specimen of urine contained only 4 g. of sugar. However, within a few weeks of discharge two 24-hour specimens of urine contained 56 and 31 g. of sugar respectively. It is our impression that bad parental supervision adds to the difficulty of achieving out-patient control.

Discussion

The evidence that good diabetic control plays an important, if not the most important, part in the prevention or postponement of the late complications of diabetes mellitus is strong (Lawrence, 1950; Joslin *et al.*, 1952; Dunlop, 1954; Engleson, 1954; Matthews, 1954). The problem is to obtain such control with the minimum of inconvenience to the patient. Any method involving only one daily injection has a great advantage in the management of diabetes, particularly in children. In the past it has been possible to control a minority of children whose insulin requirements were low by a single injection of G.I. given before breakfast, but for the majority the action of G.I. was too short and early morning hyperglycaemia occurred. In Priscilla White's (Joslin *et al.*, 1952) experience one-third of juvenile patients can be controlled with a single injection of N.P.H. insulin, which is a suspension of crystalline P.Z.I. We have no experience with this substance. In our hands a single injection of P.Z.I. mixed with S.I. had been the most useful method of achieving good control. However, this method has three disadvantages apart from the trouble involved in making such mixtures (Murray and Wilson, 1953):

1. The varying excess of protamine in P.Z.I. (Nabarro and Stowers, 1953), resulting in varying amounts of S.I. being converted into P.Z.I.

2. The error inherent in any method involving the mixing of two insulins in the same syringe. This disadvantage applies particularly to children, who should be encouraged to give injections at as early an age as possible, but who cannot be relied upon to make an accurate mixture.

3. The danger of early morning hypoglycaemia, which often necessitates a late evening meal or snack. For children such a late meal is undesirable.

These disadvantages led us to try the new insulins. In adults I.Z.S. has been found the most useful (Lawrence, 1950; Lawrence and Oakley, 1953; Murray and Wilson, 1953; Oakley, 1953; Melton, 1954). Venning (1954) obtained good results with I.Z.S. alone in 20 out of 29 patients. Ferguson (1954) was able to maintain good control in 12 out of 15 children with I.Z.S. However, in 3 of the 12 he found it necessary to add I.Z.S. (crystalline) to I.Z.S. to prolong the effect; he suggests that some of his earlier cases might have benefited from a similar addition. Two of his cases were stabilized on a mixture of I.Z.S. and I.Z.S. (amorphous). Thus less than half of Ferguson's cases were well controlled with I.Z.S. alone. By contrast we obtained good results with I.Z.S. in 18 out of 20 patients; in the other two there is no reason to believe that the addition or substitution of crystalline or amorphous I.Z.S. would have led to better control. The reason for this difference between Ferguson's and our findings probably is that Ferguson, in order to be able to compare the control obtainable with two daily injections of S.I. and with one of I.Z.S., used a fixed diet with the four main meals containing roughly equal amounts of carbohydrate and calories, while in our series good control was achieved by redistributing the carbohydrate between the various meals.

Nabarro and Stowers (1953) suggest that though the 3/7 mixture of amorphous/crystalline I.Z.S. in I.Z.S. may be optimal for Danish dietary habits, a ratio of 2/8 would be more suitable for this country. Venning (1954), however, concludes that no single mixture containing different proportions of amorphous and crystalline I.Z.S. would be likely to provide adequate control for a greater proportion of diabetics than the 3/7 mixture of I.Z.S. Our findings agree with Venning's.

In this series the amount and the distribution of carbohydrate between the various meals have been regulated according to the child's appetite and the urine and blood-sugar findings. The ratio of carbohydrate taken at breakfast, mid-morning snack, and dinner to that taken later in the day usually worked out at 3:2. In Ferguson's series this ratio was roughly 1:1, and this probably accounts for several of his cases requiring the addition of I.Z.S. (crystalline).

Nabarro and Stowers found I.Z.S. unsatisfactory in 10 out of 19 patients requiring more than 48 units a day. On the other hand, Venning achieved satisfactory results with I.Z.S. in 8 out of 13 patients who required more than 48 units. Six of our cases required more than 48 units of insulin a day, and each was well controlled with I.Z.S. (see Table). We were often pleasantly surprised at the good 24-hour control finally achieved, even though the results of early urine tests, on a smaller dose of insulin, had suggested that I.Z.S. would not prove capable of controlling glucosuria without causing hypoglycaemia at some time during the 24 hours.

Reports dealing with adults and children agree that hypoglycaemic reactions with I.Z.S. are few, that they occur commonly in the late morning or afternoon, that they tend to be typical but mild and with a gradual onset, and that usually they are easily avoided by minor dietary adjustments (Lawrence and Oakley, 1953; Nabarro and Stowers, 1953; Oakley, 1953; Ferguson, 1954; Venning, 1954). We have encountered few hypoglycaemic reactions, and only one that gave rise to anxiety (see report of Case 20). Like Murray and Wilson (1953) and Melton (1954) we have occasionally found low blood sugars not associated with hypoglycaemic symptoms. Probably the remarkably even hypoglycaemic action of I.Z.S. (Gerritzen, 1953; Murray and Wilson, 1953; Ferguson, 1954; Venning, 1954) accounts for the absence of such symptoms. It is important to be aware of these low blood-sugar levels and to make the necessary alterations in insulin dose and/or carbohydrate intake.

In previous studies local reactions due to sensitivity to I.Z.S. have been absent (Murray and Wilson, 1953; Nabarro and Stowers, 1953; Oakley, 1953; Ferguson, 1954) or infrequent (Melton, 1954; Venning, 1954). We have not encountered local reactions.

Melton suggests that if the dose of the old insulins was large, the transfer to I.Z.S. should be gradual. Venning has not yet decided whether a gradual transfer has an advantage over an abrupt one. In our series, as in Ferguson's, the change has been abrupt in every case, and we have no reason to regret this method.

In all but two cases stabilization on the new insulin took place in hospital, and it is probable that this accounts for the absence during stabilization of episodes of ketosis on the one hand and severe hypoglycaemic reactions on the other. Venning stresses the difficulties of a change-over to I.Z.S. controlled from the out-patient department and suggests certain precautions. In our opinion children

should, in general, be admitted to hospital for stabilization on the new insulins. In the two out-patients frequent attendances over a long period were necessary before good control was achieved.

Like FitzGerald *et al.* (1954) we found that transfer from a mixture of P.Z.I. and S.I. or G.I. to I.Z.S. necessitated an increase in dose. This increase reflects, at least in part, a better 24-hour control, but Venning has shown that even a well-controlled patient may need an increased dose after transfer to the new insulin to maintain a comparable degree of control. Similarly, in Ferguson's series 6 out of 10 well-controlled children required more insulin when changed to I.Z.S., and only one a smaller dose.

We agree with Venning that estimation of the 24-hour urinary sugar excretion is a most useful method of assessing control after discharge from hospital. In several children routine twice-daily urine tests before breakfast and the evening meal showed no sugar or only a trace, but the amount of sugar excreted in 24 hours exceeded 10 g. and indicated the need to increase the dose of insulin.

We adopted this method for the first time in the present study, and it has taught us that, though in the majority of diabetic children it is relatively easy to establish good control in hospital, it is much more difficult to maintain such control over prolonged periods at home.

Summary

A single daily injection of insulin zinc suspension (a 3/7 mixture of amorphous/crystalline I.Z.S.) achieved good diabetic control in 18 out of 20 children.

We are grateful to Professor J. M. Smellie and Drs. C. G. Parsons, W. H. P. Cant, and J. W. Gerrard for allowing us to study their patients; to Mr. H. B. Salt and the staff of the biochemical department, Children's Hospital, Birmingham, for the sugar estimations; and to the house-physicians and nursing staff, in particular Sister N. E. Howells, for the care of the patients. We also wish to thank Messrs. British Drug Houses and Evans Medical Supplies Ltd. for the supplies of I.Z.S. before it became generally available.

ADDENDUM.—While preparing this paper we have had the opportunity of studying a further eight children, in all of whom good control was obtained in hospital with a single daily injection of I.Z.S. It is too early to state whether such control will be maintained as out-patients.

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The first secondary technical school for deaf boys to be opened in Britain will begin the September term with thirty boys over 11 who use speech as their normal means of communication. To be known as Burwood Park School, the school is to train pupils for technical schools, technical colleges, and colleges of art. It will be under voluntary management, and is to be recognized by the Ministry of Education. Lady Patricia Lennox-Boyd and her father, the Earl of Iveagh, have given the freehold of the property to the school.

TRICHOPHYTON SULPHUREUM RINGWORM

INFECTIONS IN AN ADULT SCALP, A NEWBORN INFANT, AND THREE NURSES

BY

DENIS SHARVILL, M.R.C.P.

Dermatologist to the South-East Kent Group of Hospitals; Formerly Senior Registrar, King's College Hospital, London

The following cases of ringworm infection are of interest because one of them occurred in an infant 10 days old—possibly the youngest case on record—and because of the light the outbreak throws on the incubation period of the disease.

Case 1

This baby was born on December 19, 1953, three weeks premature, after a normal delivery. On the tenth day he was transferred to an isolation ward because of umbilical sepsis, which was readily controlled by chlortetracycline cream. His mother was definite that a rash was present on his face at this time; it was noted in writing by the resident medical officer on the fourteenth day as of a circinate erythematous nature. This caused little concern at the time and was diagnosed as "mucous burns." Dermatological opinion was not sought until the twenty-sixth day, when Dr. D. I. Williams made a clinical and microscopical diagnosis of ringworm, which he kindly invited me to investigate further on the next day.

The child was small but healthy. Three striking circular lesions were present on the face. They were bright red and scaly, with central clearing, without vesiculation or accentuation at lanugo hair follicles; one of these rings involved the eyebrow area. The scalp appeared entirely normal; the sides of the face, including the affected area, bore a luxuriant lanugo beard 1 cm. long. The limbs and trunk seemed to be normal. There was no fluorescence of scalp or face under Wood's light.

Case 2

The mother, aged 19, was seen at the same time as Case 1. Her menstrual history had been entirely normal, and this was her first child. She had lived in London for two years, and before that in a seaside town in Sussex. Two years previously she had suffered from multiple boils and whitlows; following a whitlow six months later she noticed deformity of her left index nail. For the past year there had been patchy hair loss, which worried her little; it had been diagnosed as alopecia areata, and she had used several local applications with little effect. A younger brother, still resident in Sussex, was said to suffer from boils and inflammation of the neck, but this was not investigated. Her husband was well. No other relative or close contact was known to have suffered hair loss or ringworm.

The nail of her left index finger was seen to be fragmented, but very little thickened or discoloured; there were no scars suggestive of old whitlows. At first sight the scalp was normal, except for some thinning in the left frontal and parietal areas, consisting of irregular patches of incomplete baldness on each side of the parting. Only on the closest inspection could one see broken-off stumps resembling "exclamation mark" hairs, and some black dots; these were present not only in the bald areas but all over the otherwise normal scalp. There was no inflammation or appreciable scaling, perhaps because she had been applying a lotion containing salicylic acid. Her skin was otherwise normal except for a nondescript crusted lesion 5 mm. in diameter above the left eyebrow. Removal of the crust left a shallow pit, which disappeared in ten days without treatment.

Other Cases

I was asked to see a staff midwife at the same time as the above cases. She had a scaly circinate lesion of the front and inner surface of the left upper arm covered with gentian violet, scrapings from which showed abundant mycelium. She had been in contact with the mother while in the maternity ward for 23 to 13 days before her rash appeared, and had bottle-fed the baby during the last five days of this period.

Subsequently two other nurses developed typical tinea circinata on their left arms. These two had worked only in the isolation ward and had had no contact with the mother; they had fed the baby from 15 to 7 days before their rashes appeared. In all three nurses the lesions corresponded precisely with the area of contact with the baby's right cheek during feeding: they cleared rapidly with local fungicides.

Investigations and Treatment

Potash preparations from the baby's face showed mycelium. Both at the first visit and later lanugo hairs plucked from infected areas were normal. Fungus was also found in the mother's nail and in the crust from her forehead; hair stumps showed an endothrix infection.

Positive cultures were readily obtained from all these areas on Sabouraud's dextrose agar, malt extract agar with tellurite, and penicillin-streptomycin cyclohexamide agar (Georg, 1953; Sharvill and Talbot, 1954). The fungus grew rapidly on Sabouraud's medium at 22° C., growth becoming visible in three days and reaching a diameter of 1 cm. in a week. While the colonies were flatter and less crateriform than usual, and of a dull buff rather than a bright yellow colour, slide culture identified the organism as *Trichophyton sulphureum*. The mycelium was broken up by numerous chlamydospores and hyphal swellings, microconidia were borne along the sides of the hyphae, and no macroconidia were seen.

Biopsy of the mother's scalp showed the endothrix spores; there was a small amount of dermal infiltrate, mostly periappendicular, consisting almost entirely of plasma cells with small numbers of lymphocytes and reticulo-endothelial cells.

Case 2 was treated for three months with local applications to the scalp, including kerionizing ointments, "asterol" (2-diethylamine-6-(β-diethylaminoethoxy)-benzothiazole) tincture and ointment, and Whitfield's ointment. (ung. acid. benzoic. co. *B.P.C.*) without benefit. *X*-ray epilation was then carried out, there being no signs of relapse six months later. The affected nail was avulsed and allowed to grow under chrysarobin ointment; this it did entirely normally.

The baby's face was treated with half-strength and later with full-strength Whitfield's ointment. It was normal after six weeks, and remained so up to the age of 9 months, when last seen. The scalp did not become infected.

Discussion

Ringworm in infancy is uncommon in civilized countries, as was noted by Sabouraud in 1910, when he mentioned two cases of tinea capitis in infants aged 12 and 15 days, both confirmed microscopically and culturally. Radcliffe-Crocker (1903) mentioned a case of tinea capitis at 9 days and one of tinea corporis at 7 days, but gives no mycological details, although he was well acquainted with the microscopical and cultural diagnosis of ringworm. King *et al.* (1953) described 10 cases of ringworm in infants under a year; their youngest were 3 weeks (two cases), 6 weeks, and 8 weeks (three cases); none of these was infected by *T. sulphureum*. In a review of the literature of the past twenty years they collected 11 further cases, of which only two were under 3 months; one of these, described by Lynch in 1876, had a lesion six hours after birth diagnosed clinically as tinea circinata, while another at 17 days lacked cultural confirmation. Omitted from this review are the cases of Beare and Cheeseman (1951), who described an *M. audouini* infection at 4 weeks and an *M. canis* lesion which appeared on the face of a 12-day-old boy ten days after being placed on a pillow vacated by an infected kitten. Bereston and Robinson (1953) described an *M. audouini* infection of the face and scalp in a 4-weeks-old negro baby.

The present case is the youngest patient with trichophyton infection that I have been able to trace, and if the mother's evidence is to be believed, as I think it is, it is even earlier than Beare and Cheeseman's microsporon case.

Scalp ringworm in adults is rare in Britain, although isolated cases are shown from time to time at meetings. It is, of course, commoner in eastern Europe and the Far East; thus Maschkilleisson (1936) described 53 personal cases of trichophytosis of the scalp in persons over 18 in Russia, and collected more than 600 from the literature. While it was considered rare in the United States, Pipkin (1952) suggested that it was commoner than usually supposed, since 106 dermatologists replied to his questionary with details of 258 cases. His own series of 1,304 cases of tinea capitis included 64 (4.9%) occurring after puberty; in 39 of these, all confirmed culturally, the patients were more than 20 years of age, 22 being 30 or over at the time of onset.

T. sulphureum is one of the less commonly encountered dermatophytes in Britain, although it is perhaps becoming commoner. Walker (1950) obtained *T. sulphureum* 39 times from 2,473 cultures; this was at a reference laboratory. From a personal series of 250 consecutive culturally positive cases of ringworm attending this hospital I have isolated it three times, excluding the present cases, in the past three years. Partridge (1952) found it in 15 of 179 cases of tinea capitis and in 7 of 109 cases of tinea corporis, but this, too, was in an institution working largely as a reference laboratory. Such figures may indicate an incidence higher than actually exists in London.

Beare and Cheeseman (1951), in Northern Ireland, found *T. sulphureum* in 21 of 1,004 cases of tinea capitis, which included epidemic *M. audouini* infections. Beare suggests (personal communication) that adult scalp infections with this organism are not uncommon and that they are often missed.

Many papers (Georg, 1952; Howell *et al.*, 1952; Scully, 1952; Simon and Schwartz, 1953) point to the increasing frequency of these infections in the United States. Pipkin (1952) found it in 22 of 57 adult and adolescent cases of tinea capitis, and other trichophyta of the group in 16 more. Mullins (1954) describes the examination of 3,365 schoolchildren in Phoenix (Arizona): 32 of these had tinea capitis, due in three cases to *T. sulphureum*. In 1952 Howell *et al.* discussed the clinical and pathological features and geographical distribution of 44 cases of tinea capitis due to *T. tonsurans* (*sulphureum* and *crateriforme*) in Texas and California. Family epidemics were described by Kligman and Constant (1951) and by Scully (1952). Reiss (1954) found *T. tonsurans* 44 times in 664 cultures; in 29 of these cases infections were confined to the scalp and in 11 to the skin. He drew attention to the increasing frequency of these infections in the eastern United States.

The present small outbreak is additionally interesting because of the light it throws on the incubation period of the naturally occurring disease. In the baby it could not have been more than 14, and may have been only 10 days; in the first nurse it was between 23 and 13, probably between 17 and 13, and in the other two between 15 and 7 days. This suggests that the incubation period of tinea corporis due to *T. sulphureum* is between 13 and 15 days; thus in the baby the rash appeared almost as early as it could have done, although Beare and Cheeseman's case suggests the possibility of an *M. canis* infection becoming visible as early as the second day.

Summary

A case of tinea circinata is described in a 10-day-old infant; the 19-year-old mother suffered from tinea capitis and tinea unguium. Three nurses attending the baby were infected.

Trichophyton sulphureum was isolated from the baby and from his mother.

Ringworm in infancy, tinea capitis in adults, and *T. sulphureum* infections are discussed and the literature is briefly reviewed.

The incubation period of *T. sulphureum* infections is discussed with reference to these cases.

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TREATMENT OF ASCARIASIS IN CHILDREN WITH PIPERAZINE ADIPATE

BY

M. HANNA, M.D., D.Ch.

AND

A. H. SHEHATA, M.D., D.Ch.

Cairo University, Children's Hospital, Mounira, Cairo, Egypt

Great progress in the treatment of ascariasis was attained by the discovery of the anthelmintic properties of piperazine. Many of its derivatives—namely, the hydrate, citrate, and diphenylacetate—have been tried with a variable degree of success.

Treatment with piperazine hydrate was first described by Fayard (1949), who treated about 2,000 adult cases with two 1.5-g. doses of piperazine (corresponding to 3.5 g. of piperazine hexahydrate)—one in the evening and the other the next morning. Of these cases, 70–95% passed ascarides on the second and third days. As stool examinations were not carried out after treatment it is impossible to determine the exact cure rate in this series. White (1954) reported the successful treatment of three ascaris-infested children with piperazine hydrate. He used 68, 30, and 81 mg./kg. body weight a day respectively for seven to ten days. The worms were expelled on the second and third days. Brown (1954) treated 51 cases of ascariasis with a syrup containing piperazine hexahydrate, given for two to five days. He used 1 g. a day for children weighing less than 60 lb. (27 kg.). He reported 100% cure for those who were treated for five days, 87% cure for those treated for four days, 93% cure for those treated for three days, and 85% cure in those treated for two days.

Neurological side-effects, mostly in adults, have been reported following the administration of piperazine hydrate (White and Standen, 1953; Sims, 1953). These included giddiness, lack of co-ordination, sickness, inability to focus vision, and a sense of detachment. Furthermore, the wide use of piperazine hydrate is not quite practicable, because it is a strongly basic substance and its keeping qualities in solution are uncertain.

Brown and Sterman (1954) treated 23 cases of ascariasis in children with piperazine citrate. Nineteen were cured after a single course of treatment, based on stool examination. The dose was determined on the hexahydrate content of the syrup employed.

Savaton-Pillet (1954) used the diphenylacetate salt of piperazine in treating 80 cases of oxyuris and ascaris infestation, and reported success in 73 cases with a dosage of 0.075 g./kg. body weight a day for seven days. This piperazine salt has the following disadvantages: (1) it contains 25% piperazine, so that the required dose is larger; (2) it has a distinct urinary odour, which renders it unpalatable to many patients; and (3) as a liquid preparation it is difficult to keep stable for storage.

Davies *et al.* (1954) have sought for a derivative of piperazine of low solubility, as such a compound might undergo slower absorption in the gut than the readily soluble hydrate, citrate, etc., thus avoiding the neurotoxic effects accompanying the use of the more soluble piperazine compounds. Piperazine adipate proved able to satisfy the pharmaceutical requirements considered necessary. Clinical trials in oxyuris infestation in man showed it to be completely effective and without any toxic side-effects. It was tried by Sloan *et al.* (1954), and proved an effective curative agent against a variety of helminth infections in domestic animals. Its main advantages over the hydrate are: (1) its anthelmintic effect is much greater than that produced by an equivalent weight of piperazine hydrate; (2) it is free of toxic side-effects; (3) it is stable on storage; (4) it has a high piperazine content; and (5) it has a pleasant acidulous taste and is free from odour.

While these trials were in progress O'Brien (1954) reported briefly two cases of young children whom he treated for oxyuris infestation and in whom ascarides were also present. He gave 300 mg. of piperazine adipate twice daily for six days, and in both cases the drug appeared to be strikingly effective.

Rearden (1954) also reported his experiences with piperazine adipate in the treatment of ascariasis in children and confirmed its efficacy. The dose used was 0.3 g. each day for each year of life in children up to 6 years—those over 6 were given 0.6 g. three times a day. Administration was continued for one week. All the children, save one, were completely cured.

Present Work

Piperazine adipate was used in a series of cases in order to determine the most effective dose and the number of days during which this dose should be administered in order to obtain complete eradication of ascaris infestation.

The series consisted of 85 children (47 males and 38 females) aged 1½ to 12 years, who were admitted to the Children's Hospital (Cairo University, Mounira, Cairo). The following investigations were carried out in every case: complete blood examination before and one week after treatment; blood pressure before, during, and after treatment; full examination of urine before and after treatment; and stool examinations before, and two days, four days, seven to ten days, and 14 to 30 days after treatment.

Ascaris ova were found in the stools in all cases; ancylostoma were also present in 13 cases; *Giardia lamblia* in four cases, and *Hymenolepis nana* in three cases.

The following three dosage schedules were applied: (1) 0.3 g. (one tablet) a day for each year of life up to 6 years, and 1.8 g. (six tablets) a day from 6 years upward. This was given to 25 cases. Five children received the dosage for seven days, six for five days, and 14 for three days. (2) 0.6 g. a day for each year of life up to 6 years, and 3.6 g. a day from 6 years upwards—that is, double the dosage administered to Group 1. Twenty-one cases, including two failures from the previous group, were treated for one day. Eleven cases, including four failures from the preceding cases, were treated for two days. (3) 0.75 g. a day for each year of life up to 6 years, and 4.5 g. a day from 6 years upwards. Thirty-five cases, including one failure from the second group, were treated for one day.

Treatment consisted solely of the administration of tablets of piperazine adipate as described above; no special diet was recommended during treatment. No pre-treatment measures were undertaken. The daily dose of the drug was given in three or four equal portions during the day, at four-hourly intervals, after meals. A mild saline purge was given on the day after the completion of treatment.

Results

Group Treated with Schedule 1.—The five cases treated for seven days and the six cases treated for five days were completely cured. Most of the worms were expelled on the second and third days of treatment. The worms were intact; some were still living. Ancylostoma infestation persisted in four cases. Twelve of the 14 cases treated for three days were completely cured, giving a cure rate of 85.7%. In one case the first stool examination two days after treatment still showed a few ascaris ova, but was subsequently negative. This patient passed only one ascaris worm on the fourth day from the start of treatment. Another patient passed many ascaris worms from the third to eighth day; stools, however, still contained ascaris ova. A second similar course was given seven days after the first course, but no worms were expelled and stools were still positive for ascaris ova. In two cases ancylostoma and *Giardia lamblia* infestations were not affected.

Group Treated with Schedule 2.—Of the 21 cases given the treatment for one day 17 were completely cured, including the two failures from the previous group, showing a cure rate of 80.9%. The same course was repeated after seven days in three out of the four failures in this series, and though they again passed ascaris worms the stools still contained ascaris ova. The fourth case in which the infection persisted passed 72 ascaris worms on the first and second days of therapy. In six cases acylostoma and *G. lamblia* infestations were not affected. Among those treated for two days (11 cases) there was only one failure, the cure rate being 90.9%. The failure responded to schedule 3 dosage (see below). In two cases ancylostoma and *G. lamblia* resisted treatment.

Group Treated With Schedule 3.—All the 35 cases in this group were completely cured, including the resistant case which had previously received three courses. In seven cases ancylostoma and *Hymenolepis nana* were not affected.

Side-effects.—No toxic effects or side-reactions were noted in any of the cases, although some of them received repeated courses of treatment. There was no demonstrable effect on the kidneys, the circulatory system, or the blood picture.

Summary and Conclusions

A series of 85 children (47 males and 38 females), aged from 1½ to 12 years, suffering from ascaris infestation were treated with piperazine adipate tablets, each containing 0.3 g., according to the plan described.

As a result it can be definitely stated that piperazine adipate is a very effective and safe drug for the treatment of ascaris infestation in children. The recommended schedule, especially for wide use, is a dose of 0.75 g. for each year of life up to 6 years and 4.5 g. from 6 years upwards, to be given for one day in four equal doses at four-hourly intervals, after meals.

Piperazine adipate was given in the form of tablets, which were easily taken by children. The tablets were administered whole in most cases, but in some it was necessary to crush them; this presented no difficulty. The tablets were not objected to by the children whether given whole or crushed.

The piperazine adipate used in these investigations was kindly supplied by British Drug Houses Ltd. as "entacyl" tablets.

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Medical Memoranda

Ferrous Sulphate Poisoning with Gross Stricture of the Stomach

To illustrate the destructive effects following ingestion of ferrous sulphate pills, and to stress further the criminal negligence in leaving such pills within the reach of small children, the following case is briefly reported.

CASE REPORT

A male child of 20 months swallowed approximately 50 "fersolate" tablets and was admitted to hospital two hours later. An unrecorded proportion of the pills was recovered by immediate gastric lavage. There was repeated and severe haematemesis. The initial collapse was treated successfully by blood transfusion, but during the next few days there was a steady deterioration in the general condition, and it was not possible to maintain nutrition adequately by mouth because of repeated vomiting. When seen seven weeks after the onset of illness the child was found to be emaciated and dehydrated.

A barium meal showed a smooth tubular stricture affecting the middle third of the stomach (see Fig.).

The child was transferred to a paediatric unit in the hope of improving his nutrition and of preparing him for operation. Despite feeding by an intragastric tube, which was passed beyond the obstruction, and by the intravenous route, there was a progressive decline, and at no time did he seem fit for surgery. A further barium meal showed progressive and irregular stricture formation. He died 16 weeks after poisoning.

The necropsy showed dense adhesions in the upper peritoneal cavity. A small pouch of healthy stomach proximally

and a normal pyloric antrum were found. The intervening stomach showed gross inflammatory changes, and a narrow channel was lined with granulations, ulcerated and adherent to surrounding organs. A large chronic ulcer penetrated the liver at one point. The muscle wall was replaced by fibrous tissue. The liver and kidneys were normal. These appearances confirmed that excision of the stomach would have been almost impossible in the last weeks of the illness.

COMMENT

There have been numerous reports in recent years of the corrosive effects of ferrous sulphate poisoning. Forbes (1947) and Thomson (1947) drew attention to the hazard of leaving attractive sugar-coated pills accessible to infants and children. Further cases have been described by Prain (1949), Spencer (1951), Crosskey (1952), Ross (1953), and Elliot-Smith and Davies (1954). Forshall and Rickham (1954) have discussed fully the complication of pyloric stenosis after ingestion of ferrous sulphate pills. Stricture of the mid-portion of the stomach, as found in the present instance, is less commonly encountered, and presents a more difficult problem of management than does a localized pyloric lesion.

If a child survives the immediate prostration and toxicity due to a heavy dosage of ferrous sulphate the mucosal changes in the stomach are apt to be severe and the subsequent contracture and ulceration progressive. Repeated haematemesis is probably an indication of excessive mucosal damage. It would appear that early operation is necessary, and it is suggested that jejunostomy should be performed as soon as possible. This should be followed by early resection of the stomach unless repeated radiological examination shows rapid improvement in the local condition. These contentions are borne out by the experience of Ross (1953), who described a somewhat similar case.

Dr. C. H. Stewart-Hess referred the child to me, and I am indebted also to Miss Isabella Forshall, to whom I transferred him for further treatment, for details of the later stages of the illness.

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JOHN A. SHEPHERD, V.R.D., M.D., Ch.M., F.R.C.S.Ed.,
Surgeon, Broadgreen Hospital, Liverpool.

A Case of Priapism

Priapism is defined as continuous erection of the penis without sexual stimulation. It is an uncommon condition and is not very adequately dealt with in the textbooks. As the patient attended on a Sunday morning one was denied access to the literature.

CASE HISTORY

On August 23, 1953, a boy of 13 was admitted to hospital. While playing football about 40 hours previously he had been kicked accidentally in the perineum. A few hours later he was taken to his doctor's surgery complaining of lower abdominal pain and vomiting. He did not at that time mention the kick, and apparently it was thought then that he probably had mild appendicitis. He was not referred to hospital until the following day, by which time he had had intense priapism for about 16 hours, with dysuria.

On examination his penis was erect and extremely tender, as was the perineal region. No evidence of bruising was found, but direct questioning disclosed the history of trauma. His temperature was 103° F. (39.4° C.) and pulse rate 104. The bladder was distended to about half-way between the symphysis pubis and umbilicus at the beginning of the examination, but he managed to pass 13 oz. (370 ml.) of urine after rectal examination, which was very painful owing to the congestion of the corpora cavernosa. The urine was clear. The spleen was not palpable and a blood examination did not disclose leukaemia. No positive findings were made on routine examination of other systems. A diagnosis of priapism due to mechanical obstruction of the efferent veins from the penis caused by oedema or thrombosis due to the trauma was made.

A low spinal anaesthetic was administered without any effect on the priapism. It did, however, relieve the pain temporarily. Any element of venous spasm thus being eliminated, the fact of mechanical obstruction was established.

Aspiration or incision of the corpora was decided against, as we considered that as the priapism had been present for only 16 hours thrombosis in the corpora should not have occurred and could be logically prevented by anticoagulants.

Treatment by heparin and ethyl biscoumacetate was begun, being controlled by daily prothrombin activity estimation. Adequate sedation was also administered in view of the severity of the pain.

The patient had considerable difficulty with micturition, but once the stream started the bladder emptied. Catheterization was avoided. On the second day he volunteered that micturition was easier, though there was no apparent alteration in the priapism. By the third day the temperature had settled spontaneously. On the sixth day he said that he now thought the penis was softer, and this was confirmed. By the twelfth day the penis was quite flaccid but still larger than it had been before the accident; micturition was normal. On the fourteenth day he was allowed up, but it was noticed that, although the corpora were quite soft, there was a tender spot in the right corpus in the perineum. It was considered that this was probably the site of the original trauma and would resolve spontaneously. Anticoagulants were discontinued. By the seventeenth day the prothrombin activity was within normal limits and the patient was discharged home. He was seen at the follow-up clinic on October 8, when it was found that the penis was normal in size and shape. As he has not reached the age of active sexual life no effect on this important function could be recorded.

COMMENT

Search of the literature has shown that only one case of priapism treated by anticoagulants (dicoumarol) has been recorded (Smith, 1950). Prior to this, aspiration and incision of the corpora were advised by several surgeons. Calloman (1950), in his exhaustive review of the condition, gives a good prognosis, whether or not active surgery is employed. Some authors (Kemp and Hosay, 1950) report impotence due to organization of clots in the corpora cavernosa. In one patient operative release of fibrous tissue at the base of the penis was required owing to persistent partial priapism and lack of erection during sexual stimulation. It would appear that this distressing sequel has been avoided in the case recorded, as no thickening can be felt in the perineum which might result in impotence.

The treatment of priapism with anticoagulants seems to have been entirely successful and would certainly appear to be the most rational despite Calloman's remarks.

My thanks are due to Mr. F. Mitchell Heggs, under whose care the patient was admitted, for permission to publish the case.

W. J. FRASER, M.B., F.R.C.S.Ed.,
Senior Registrar in Surgery, City General Hospital, Sheffield.
Late Senior Registrar in Surgery, Bury and Rossendale Hospital Group.

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Reviews

COLLECTED PAPERS OF OTTO FENICHEL

The Collected Papers of Otto Fenichel. Second Series. Collected and edited by Hanna Fenichel and David Rapaport. (Pp. 374+viii. 35s.) London: Routledge and Kegan Paul Ltd. 1955.

Fenichel would certainly rank among the first dozen, or perhaps even half-dozen, of the leading psycho-analysts of the past 30 years. His standard work, *The Psychoanalytic Theory of the Neuroses*, is one of the three or four classics of psycho-analytical exposition and is not surpassed by any. His encyclopaedic knowledge of the literature combined with a critical estimation of the various contributions, his extensive experience in both practice and teaching, together with a clear brain and sound judgment, made him one of the best exponents of this difficult subject.

In the two volumes of his collected papers we have his more individual contributions to the theory and practice of psycho-analysis. They range over a vast field and throughout disclose an undeniable originality. The present volume, the second in the series (the first was reviewed in these columns on February 12 last), contains what he wrote in the last 24 years of his life. The quality of this excels that in the first volume, as one would expect from his ripened experience. Fenichel was one of those whose capacity improved after he emigrated to America, which is far from true of all those who did; perhaps the climate of California proved more congenial than that of New York. He was easily the leading analyst in the west of America, and was subject to fewer of the distractions to be met with in the eastern States.

In this second volume there are 27 chapters. Perhaps the most valuable are the half-dozen dealing with what is nowadays termed ego psychology, which are of outstanding importance. A review of a book by Erich Fromm displays Fenichel's critical capacity at its best. A fascinating paper entitled "The Misapprehended Oracle" is a penetrating study of the wish-fulfilling tendencies that distort favourable predictions, the story of Macbeth being chosen to illustrate the mechanism concerned. A final chapter on Freud's place in science is only too short and by no means adequate. In it he wrote the very true words: "In seeking to implement his practical needs of a physician treating hysteria, Freud discovered and developed the science of psychology. Compared to this fact the therapeutic application of psychoanalysis pales into insignificance."

The hackneyed remark, "This book should be on the shelves of every psycho-analyst," is much truer here than it often is. But it is a book that should regularly leave the shelves, since there is no student of psychopathology who would fail to obtain constant stimulation from its perusal.

ERNEST JONES.

ANATOMY OF THE CENTRAL NERVOUS SYSTEM

The Neuroanatomical Basis for Clinical Neurology. By Talmage L. Peele, M.D. (Pp. 564+ix; illustrated. £5.) New York, Toronto, London: McGraw Hill Book Co. Inc. 1954.

The author, who is associate professor of anatomy in charge of neuroanatomy and assistant professor of medicine at Duke University School of Medicine, has used this combined experience to excellent purpose in the writing of this book. The basis of the book is a detailed account of the anatomy of the central and autonomic nervous systems with clear diagrams and first-class illustrations of sections at various levels. The description of the anatomy of each part of the nervous system is followed by a shorter but interesting account of present-day views on its physiology and an accurate résumé of the clinical disturbances caused by lesions at that level. A notable omission is any adequate account of the peripheral nervous system. There is a chapter dealing with the histology of peripheral nerves, posterior root ganglia, and the neuro-muscular junction, but in a book with such a title one might expect a more detailed account of the distribution of the spinal segments and peripheral nerves, since lesions of nerve roots and peripheral nerves are so frequently seen in the clinical practice of neurology. This is, however, a minor criticism of an excellent book. The text is too long and detailed for most medical students, but it will be of great value to those reading for honours degrees in anatomy and physiology, and for any clinician who has more than a passing interest in disorders of the nervous system.

J. W. ALDREN TURNER.

MEDICAL SOCIAL WORK

Expanding Horizons in Medical Social Work. Edited by Dora Goldstine. (Pp. 274+viii. 37s. 6d.) Chicago: University Press. London: Cambridge University Press. 1955.

This is a companion volume to *Readings in the Theory and Practice of Medical Social Work*, also edited by Miss Goldstine, who is Professor in the School of Social Service Administration at the University of Chicago. The present volume—a collection of previously published articles—deals with the conquest of new territories by the medical social worker, and the first of the two sections reveals the nature of the struggle and the tactics which the medical social worker employs to overcome "resistance" by administrators, politicians, and doctors. Many of the articles were written in the 1930s after the experience of the slump, and this may account for the air of fanaticism with which the gospel of the social factor in illness is propagated. Some problems they mention have vanished in our welfare state, in which the basic material security of the patient can be taken for granted; and others are somewhat strange to British ears—for example, the need to safeguard patients from too severe dunning by hospital accountants.

The responsibility for ensuring that the patient is understood as a human being and that emotional factors and personal problems are appreciated by hospital staffs seems to rest at present, in the view of these writers, almost entirely on social workers, and to remedy this state of affairs they foresee a considerable task in educating doctors and medical students in the importance of the social factor in illness.

Medical readers will not altogether relish the numerous criticisms of medical attitudes which are found in the book, and they would probably prefer a presentation of the subject which was less of a sermon and more of an argument. Unfortunately, much of the criticism is justified. As Ferguson and McPhail have pointed out in their book *Hospital and Community*, much effort in hospitals has often been wasted because we have not listened enough to the message which these writers are so anxious to convey.

T. FERGUSON RODGER.

THE VISUAL FIELDS

The Visual Fields: A Study of the Applications of Quantitative Perimetry to the Anatomy and Pathology of the Visual Pathways. By Brodie Hughes, M.B., B.S., Ch.M., F.R.C.S. (Pp. 174+ix; illustrated. 35s.) Oxford: Blackwell Scientific Publications. 1954.

This book sets out the author's methods of examining the visual fields and the experience he has gained from trying to correlate these with pathological anatomy in many thousands of cases. From the point of view of a neurosurgeon, this book could not be surpassed, and among the visual field charts of illustrative cases, all of which are the personal work of the author, are to be found every variety of visual field defect that a neuro-surgeon is likely to encounter. By using continuous lines for the peripheral isoptres (as determined by the use of the perimeter) and dotted lines for the central isoptres (as determined by the use of the Bjerrum screen) the field charts have been made easy to identify. Much space has been given to the anatomy of the visual pathways and their blood supply (five chapters), and at the end of certain chapters under the heading "Conclusions" the author sums up some of the controversial problems mentioned and gives his own views.

Although Professor Brodie Hughes states that matters of primarily ophthalmic interest, such as disease of the eyes, have been given scant notice, the reviewer feels that the book would have been of greater value had chapters 13 and 14, which deal largely with ophthalmic problems, been amplified, and preferably been written in conjunction with an ophthalmologist. Such a plan might have avoided such a statement (p. 163) as: "the initial field loss in glaucoma is an arcuate scotoma," a statement which, even if the non-congestive type of glaucoma were specified, may not be universally true.

Few ophthalmologists would agree that the "papill-oedema" which may occur in hypertensive and diabetic retinopathy, and which after all is usually only part of a generalized retinal oedema, commonly gives rise to secondary optic atrophy (p. 79); and, incidentally, is the author justified in confining the use of the term "secondary optic atrophy" to the atrophy of the optic nerve which may follow "papilloedema"?

Minor points of criticism are the author's frequent use of the words "and so forth"—presumably in order to avoid someone saying, "Oh, but you have left out so-and-so!"—the failure to distinguish the abstract noun "case" from the concrete noun "patient," and the omission of the "r" in the word "macular" when it is used as an adjective as in "papillo-macular bundle." There is one mistake in the field charts, and that is in Fig. 142, where Fig. 142b should be Fig. 142a, Fig. 142c should be Fig. 142b, Fig. 142d should be Fig. 142c, and Fig. 142a should be Fig. 142d.

This book is a practical and up-to-date work on the subject of visual fields, based upon the vast experience of a neuro-surgeon who knows the value of detailed and personal attention to his patients. It is a valuable contribution to medical literature and it should stimulate others to pay greater attention to visual field studies.

T. KEITH LYLE.

COLD INJURY

Cold Injury. Transactions of the Third Conference. Edited by M. Irene Ferrer, M.D. (Pp. 226; illustrated. $4.50.) New York: Josiah Macy Jr. Foundation. 1955.

This book reports the transactions of the Third Conference on Cold Injury held at Fort Churchill, Canada, in 1954. Reports of verbal communications and discussions of them usually make difficult reading, and this report is no exception. Nevertheless, it contains much information of value to those interested in environmental research, and will be found useful as a source of reference to current literature. For the physician, the chapter of most interest is one on metabolic studies in the Eskimo. We learn that Eskimos do not suffer from rheumatic fever or rheumatoid arthritis, but show a high incidence of degenerative joint disease, and age rapidly. An obscure type of hepatomegaly is common among certain groups, who live for months of the year on seal, walrus, or caribou meat. The condition is reversible and has been shown to disappear on changing to a normal diet. Liver biopsies showed no abnormality of architecture or fat content, and tests of liver function gave normal results. There was evidence suggesting that the condition was due to hyper-vitaminosis A, the daily intake of vitamin A being of the order of 50,000 units a day. Another interesting finding among Eskimos was the presence of trichinosis, the natural host being the polar bear. In view of their large fat intake (about 65% of the total calories) a high incidence of atherosclerosis has been looked for among Eskimos, but there is as yet no conclusive evidence of it.

Studies on cold tolerance in Eskimos and Indians showed a remarkable superiority in resistance to cold injury and ability to work with the hands exposed to low temperatures, as compared with white controls. It was considered that physico-chemical factors relating to the peripheral tissues and nerves, as well as local circulatory differences, were responsible. In another paper blood flow and skin temperature in the hands exposed to cold were shown to be higher in Eskimos than in controls. Other papers deal mainly with animal experiments on fat metabolism, ascorbic acid metabolism, and diet in relation to cold acclimatization. It is curious to find, in view of its title, that this report contains hardly any material on the subject of cold injury.

G. PUGH.

A GERMAN TEXTBOOK OF ANATOMY

Rauber-Kopsch Lehrbuch und Atlas der Anatomie des Menschen. By Dr. Fr. Kopsch. 19th edition. Band II. (Pp. 768+vii; illustrated. D.M. 64.50.) Stuttgart: Georg Thieme Verlag. 1955.

We recently (July 16, 1955) reviewed the first volume of this great textbook of human anatomy, which now appears in its nineteenth edition. This second volume, including accounts of the viscera, the nervous system, and the special sense organs, maintains the same high standards. A large proportion of the illustrations are from preparations made by Professor Kopsch himself, and it is difficult to assess at their true value the perfect conception and the superb execution of the dissections involved. The artistic reproduction is of the highest order, and the result is an atlas of human anatomy in a class by itself.

The central nervous system is illustrated by a series of sections exquisitely drawn by Krause from photographs. They show the minute structure of the brain with a clarity and precision which we have never seen approached. There follows a complete set of diagrams of the nerve tracts by Bechterew and Richter, so well drawn that one almost forgets the vast complexity of the subject. The distribution of the peripheral nerves and of the sympathetic system are shown in a series of beautiful dissections.

The organs of special sense are described in great detail. The minute structure of the eye and of the ear are illustrated by coloured drawings from the microscope which are really superb.

The genius behind this great atlas is Professor Kopsch himself, for he has been associated with its production for 50 years. But inspired by him there must have been a group of assistants who grudged no effort to achieve a perfect dissection and of artists with a rare power of interpretation of complex subjects. The accompanying descriptions are brief and accurate, forming an integral part of what is essentially a visual picture of the human body. It is a very great book and it will be welcomed by all who are interested in what is, after all, one of the most fascinating of human studies.

HENRY SOUTTAR.

ELECTRICAL ACCIDENTS

Klinische Elektropathologie. I—Kritische Sammlung Elektropathologischer Gutachten aus Interner Sicht, by S. Koeppen. II—Die Neurologie des elektrischen Unfalls und des Blitzschlags, by F. Panse. (Pp. 424+ix; illustrated. D.M. 33.) Stuttgart: Georg Thieme Verlag. 1955.

Clinical Electropathology is divided into two parts. The first is described as a critical collection of electropathological opinions from the point of view of internal medicine. In this portion an account is given of the effects of electrical accidents on the vascular system. Angina pectoris is said to result from electrical trauma, the text containing details of a large number of cases. The effects of electrical shock on various disorders are considered and case histories given. Included are such diseases as peptic ulcer, Graves's disease, and diabetes mellitus. The question of diminished earning capacity resulting from electric shock is considered. The second part of the book, by another author, treats of the neurology of the electrical accident and lightning stroke. Here there is much material and 125 cases are described.

This monograph certainly provides a vast amount of carefully documented information, and should be a useful reference book for anyone interested in the subject from a medico-legal point of view or wishing to find out all that is known about the effects of electrical trauma in any particular disease or on any particular organ or system. There are full references and an index and many good (and sometimes macabre) illustrations. For the ordinary reader of the unusual there is much to interest him.

TERENCE EAST.

BRITISH MEDICAL JOURNAL
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BREATH-HOLDING ATTACKS

Breath-holding attacks are important not only because of the worry which they occasion to parents but because of their resemblance to epilepsy. They usually start in the first 18 months of life. They can begin as soon as the first week, but are almost unknown after the age of 4 years. The attacks are usually brought on by anger, thwarting, punishment, an attempt to force the child to do something against his will, or to prevent him doing something which he has set his heart on. They may result from another child snatching a much-wanted toy from him. What is not commonly recognized is that attacks may be due to pain from a fall or injury, or to sudden fear.

The sequence of events in a breath-holding attack is characteristic. The child cries as a result of one of the precipitating factors mentioned above, but then, often only after two or three cries, he holds his breath in expiration. In 5 to 10 seconds, a remarkably short time after the onset, he becomes cyanosed, and then in the great majority of cases he takes a breath and the attack is over. In a few cases the child holds his breath for a further 5 to 10 seconds, and then becomes limp, pale, and unconscious. If he holds it for a further 10 seconds or so he has a major convulsion, indistinguishable from epilepsy. There is marked bradycardia in the attack. The whole fit lasts not more than 2 or 3 minutes. After a few moments' confusion, the child appears to be perfectly normal. He may experience only one attack in a lifetime. S. Livingston[1] found that, of 242 children with breath-holding convulsions, 87 had one or more a day, and 33 had less than one a month. In all but three, attacks disappeared spontaneously by the age of 5, and in the remaining three they ceased at 6 years.

The mechanism of the attacks was explained by Sharpey-Schafer and his colleagues in this *Journal*[2] under the title "The Mess Trick and Fainting Lark." Schoolboys and others have learnt the trick of overventilating and then holding the breath in expiration, with the result that they "faint." Overventilation causes dilatation of muscle and constriction of cerebral blood vessels. The increased intrathoracic pressure produced by holding the breath in expiration causes a drop in blood pressure, and, as there is already cerebral vasoconstriction, severe cerebral anoxaemia results so that unconsciousness and perhaps convulsions occur. Bridge *et al.*[3] ascribed the apnoea to spasm of the glottis, for they noted contractions of the diaphragm during a breath-holding attack, without any effect on the ventilation or colour of the child.

Various workers have suggested that breath-holding attacks occur in a particular type of child, who has other behaviour problems. As all children have behaviour problems, little importance can be attached to this. Nevertheless, it is clear that repeated attacks are more likely to occur in mismanaged children than in those who are managed well, with sympathy and understanding, for, except those attacks due to fear or pain, repeated attacks in a child represent an excessive response to frustration, often as an attention-seeking device or as a method of getting his own way. The child who is thoroughly secure is less likely to have attacks; and the child who does not find that by having an attack he can create a great deal of fuss and anxiety, and can get his own way, is unlikely to repeat the performance—for the breath-holding is apparently voluntary and deliberate, at least in the older child, though the results of breath-holding are not. The observation made by Bridge *et al.* that 7 out of 83 cases started after an attack of whooping-cough, in which there are somewhat similar attacks of apnoea, is difficult to understand. Perhaps it was related to "spoiling" in their illness.

Breath-holding attacks are often confused with epilepsy, but it is essential to distinguish the two. As the attacks are not often seen by the doctor, the diagnosis rests essentially on a careful history. The orderly and rather slow sequence of events in the breath-holding attacks, a few cries after a known precipitating factor, followed by breath-holding in expiration, the rapid onset of cyanosis, followed by limpness and convulsions in that order, differ from epilepsy, in which fits rarely follow any precipitating factor, though it should be noted that over-ventilation, as from excessive crying, can precipitate a fit in an epileptic. In epilepsy the so-called epileptic cry before a convulsion is unusual in children, and when it does occur it is usually different in nature from the child's ordinary cry. In epilepsy the clonic phase is preceded not by limpness but by a tonic phase, and cyanosis, instead of preceding the onset of the fit, follows the beginning of the tonic spasm. The whole sequence of events in an epileptic fit is much quicker.

[1] Livingston, S., *Convulsive Disorders in Children*, 1954, Springfield, U.S.A.
[2] Sharpey-Schafer, E. P., *et al.*, *British Medical Journal*, 1951, **2**, 382.
[3] Bridge, E. M., *et al.*, *J. Pediat.*, 1943, **23**, 539.
[4] Low, N. L., *et al.*, *Pediatrics*, 1955, **15**, 595.

After an epileptic fit, the child, instead of being momentarily confused, is likely to fall asleep. Though many epileptic fits are short-lasting, some may last for many minutes or even for hours, while breath-holding attacks never last longer than two or three minutes. Breath-holding attacks bear no relation to epilepsy. Livingston[1] found a normal E.E.G. in 196 of 198 children with breath-holding convulsions. Only 2 of 242 children with such convulsions subsequently developed epilepsy. N. L. Low *et al.*[4] performed electroencephalograms during sleep on 129 children subject to these attacks, and found them normal in all but one child. One tracing during a breath-holding spell showed slow wave but no seizure activity.

Treatment is not easy. It can be stated categorically that drugs are useless. In the early stage of an attack, before consciousness is lost, a sound slap on the face or buttocks, or the splashing of cold water over his face or head, may be enough to cause the child to inspire—and the attack stops immediately one breath is taken. If the next stages cannot be averted, the essential thing is to avoid a fuss, to pay as little attention to the child as possible when he recovers, and on no account to let him have his own way as a result of the attack. If he is standing at the beginning of an attack, he must be laid down: otherwise there is nothing to do but wait for the end of the fit. Unless the attack originated from pain or fear, the underlying causes must be sought—the underlying insecurity, excessive discipline or lack of discipline, and the reason for the child's need to adopt attention-seeking devices. It is worth while considering whether the conflict of wills such as may spring from the parent's stand in insisting on a particular line of action, or in forbidding the child doing something he wanted to do, or in smacking the child, was really justified. The odds are that it was not.

DIETARY PROTEIN IN ACUTE NEPHRITIS

The diet in acute nephritis has often been the subject of controversy. Recommendations—given with great emphasis and little evidence—have ranged from normal to low protein intake; and both the quality of the protein and the colour of the meat have been questioned, the latter being considered particularly sinister if it is red but permissible if white. It has been suggested that the protein of milk is harmless.[1 2] Osler allowed his patients a liberal amount but advised that meat should be used sparingly. Moreover, there is some experimental evidence that it is not the protein which is harmful but non-protein nitrogenous substances which are present, particularly in liver and beef meat.[3]

Diets very high in protein do not appear to be injurious to normal people. T. J. Addis[4] studied the urinary sediment before and after a single meal of 1½ lb. (700 g.) of meat and found no difference. E. F. Du Bois and W. S. McClellan[5] studied two Arctic explorers, Stefansson and Anderson, who volunteered to eat nothing but meat—which they did for a year under constant observation. Their diet included meat fat as well as lean, and contained 100–140 g. of protein (the only carbohydrate was that derived from meat glycogen and was estimated to be 7–12 g. daily). No renal changes were found at the end of the study. L. H. Newburgh, M. Lesses, and M. W. Johnston[6] fed a normal man a diet which included 338 g. of protein for six months. They observed that his blood pressure and retinae remained normal, but that slight albuminuria and a fifteen-fold increase in casts, many of which were granular, appeared towards the end of the period; both these abnormalities disappeared ten days after stopping the diet. A. Krogh and M. Krogh[7] have estimated that the Greenland Eskimo consumes about 280 g. of protein daily. With this in mind, W. A. Thomas[8] examined 142 middle-aged Eskimos in Greenland. Although he concluded that the incidence of renal disease was not excessive, he found albuminuria in 8.5% (excluding cases with pus). His examination did not include microscopy in all cases and his numbers were small. A. A. Osman[9] in a follow-up of acute nephritis studied 56 cases for periods of eighteen months to twenty-two years and could find no correlation between their ultimate condition and type of diet. A. Naeraa[10] kept nine patients who had had acute nephritis under observation and gave them alternating high- and low-protein diets. In seven the Addis count of cells in the urinary sediment was unaffected, but in two a sudden increase occurred when the high-protein diet was introduced; in one of these cases this happened on two occasions. Naeraa also mentions that in some cases mild albuminuria appeared on the right-protein diet although it had disappeared when the protein intake was low. J. Rudebeck,[11] in a long-term follow-up of 194 cases, could not conclude that the diet influenced either mortality during the acute stage or the incidence of the chronic stage following the acute

[1] Osler, W., *The Principles and Practice of Medicine*, 7th ed., 1909, New York and London.
[2] Garrod, A. E., *et al.*, *Diseases of Children*, 2nd ed., 1929, London.
[3] Newburgh, L. H., and Johnston, M. W., *J. clin. Invest.*, 1931, **10**, 153.
[4] Addis, T., ibid., 1926, **2**, 417.
[5] Du Bois, E. F., and McClellan, W. S., *J. biol. Chem.*, 1930, **87**, 651.
[6] Newburgh, L. H., *et al.*, *Amer. J. med. Sci.*, 1930, **179**, 305.
[7] Krogh, A., and Krogh, M., *A Study of the Diet and Metabolism of Eskimos*, 1913, Copenhagen, quoted by Du Bois, E. F., and McClellan, W. S., *J. biol. Chem.*, 1930, **87**, 651.
[8] Thomas, W. A., *J. Amer. med. Ass.*, 1927, **88**, 1559.
[9] Osman, A. A., *Guy's Hosp. Rep.*, 1925, **75**, 306.
[10] Naeraa, A., *Acta med. scand.*, 1938, **95**, 359.
[11] Rudebeck, J., ibid., 1946, Supp. CLXXIII, Lund.
[12] Mortensen, V., ibid., 1947, **129**, 321.
[13] Farr, L. E., and Smadel, J. E., *Proc. Soc. exp. Biol. (N.Y.)*, 1937, **36**, 472.
[14] Illingworth, R. S., *et al.*, *Arch. Dis. Childh.*, 1954, **29**, 551.

attack. V. Mortensen[12] reported on 49 cases of post-scarlatinal nephritis and gave alternate cases diets low (40 g.) and high (125 g.) in protein; he found no difference between the groups, but the albuminuria ceased more rapidly in the cases on the diet high in protein.

As to experimental work, L. E. Farr[13] produced nephritic lesions in rats, and fed each group on a diet containing 5%, 18%, or 40% protein. The 40% group fared the worst. Although this experimental nephritis may not be comparable to the human disease, it is noteworthy that in the group on 18% protein, which is only slightly above the average human intake of protein, 8 out of 15 rats which survived the acute phase died at 5½ months of renal failure, while in the group on low protein 14 out of 16 completely recovered.

Thus, although in acute nephritis in man the evidence is scanty that a diet low in protein hastens recovery and a normal protein diet delays it, clinicians are naturally reluctant to depart from tradition or clinical impression until there is good evidence for doing so. This has now been supplied by R. S. Illingworth, M. G. Philpott, and J. Rendel-Short[14] in a carefully controlled study of acute nephritis in 42 children. Two comparable groups, allocated by random sampling, were treated identically except that one group was given a daily diet low in protein (average 0.3 g. per lb. body weight—0.7 g. per kg.) and the other a normal protein diet (average 1.23 g. per lb.—2.7 g. per kg.). Strict criteria for healing were adopted and included an Addis count of 500,000 or fewer red cells in the 12-hour specimen. Three months after admission the groups on low and normal protein contained five and four children in whom healing was judged to be complete. The failures numbered four in the low-protein and two in the normal-protein group, and there was one death in the low-protein group. This study therefore suggests that recovery will not be jeopardized by allowing patients a protein intake somewhere near their normal after the first few days of illness. On the contrary, the essential amino-acids thus supplied will help to preserve the nutritional state at its optimum.

HOME AND CLINIC TREATMENT OF TUBERCULOSIS

Sir Robert Philip established the first tuberculosis dispensary in Edinburgh in 1887. Its main functions were diagnosis, the making of arrangements for sanatorium treatment, and training the patient and his family in hygienic measures designed to limit the risks of infection.[1] Little out-patient treatment was given. From this beginning the dispensary idea spread, especially when in 1921 local health authorities took up the responsibility of looking after tuberculous patients. Even before the National Health Service Act transferred treatment to regional hospital boards many dispensaries had developed their functions, and in calling themselves chest clinics proclaimed a wider outlook.. Refills of pneumothorax added another form of treatment to clinic work, and many clinics also were associated with the tuberculosis wards in the local hospital. To-day boards have provided chest clinics over the whole country, the chest physician (the former tuberculosis officer writ larger) thus being orientated more towards treatment, though he is also responsible to the local health authority for the preventive aspects of his work.

The war and its aftermath produced a great demand for beds; short spells of simple sanatorium treatment, available only to favourable cases, satisfied none when prolonged rest and collapse therapy offered better results. Despite provision of more beds the demand could not be fully met, and long waiting-lists for institutional treatment arose. There have always been more patients at home under the care of the family doctor than in hospital or sanatoria, but the situation called for a new attack. Several chest-clinic physicians—for example, C. H. C. Toussaint[2]—realized that the time had come to provide more active treatment, based on home and clinic. P. Stradling,[3] a firm advocate of such treatment even to-day when beds are easier to find, describes results in 64 patients whom he treated in this way in 1948 and has followed up for five years. Stressing the advantages of domiciliary and clinic management, he claims that patients fare as well under this system as when sent away to sanatoria. He used the relatively few beds then available to him for short periods of admission—largely for "medical collapse therapy," though 75% had to be sent elsewhere for "institutional convalescence." To-day a five-year assessment of the results of treatment in tuberculosis is inadequate, but few will dispute that many patients can be successfully treated under such a plan, and that it is no longer necessary to occupy sanatorium beds with those patients who can be happily managed in domestic circumstances. Chemotherapy is a valuable adjunct to domiciliary management, and, even if the patient needs admission to hospital later, is a sound preliminary to further treatment. Careful co-ordination of all the facilities available is an important function of the clinic; in addition to specialist medical advice and supervision, the patient may need the help of the almoner, district nurse, tuberculosis health visitor, home helps, ambulance, and other local health authority services.

The family doctor can thus again join in the active treatment of his tuberculous patient, for domiciliary and clinic management requires the close co-operation of chest physician and general practitioner. Under Stradling's plan patients may be admitted for short periods to the local hospital tuberculosis ward. P. Forgacs[4]

[1] Philip, R. W., *British Medical Journal*, 1904, **1**, 1357.
[2] Toussaint, C. H. C., *Domiciliary Management of Pulmonary Tuberculosis (Bishop Harman Prize Award, B.M.A.), Trans. med. Soc. Lond.*, 1950, **67**, 36.
[3] Stradling, P., *Tubercle (Lond.)*, 1955, **36**, 150.
[4] Forgacs, P., ibid., 1955, **36**, 109.
[5] Mitchell, R. S., *Amer. Rev. Tuberc.*, 1953, **67**, 401, 421.
[6] Report of B.T.A. meeting, *Tubercle (Lond.)*, 1954, **35**, 290.

describes a modification in which special short-term hospitals were used. The value of long periods of bed-rest alone have been questioned since R. S. Mitchell's[5] analysis of the records of patients with minimal disease in the Trudeau Sanatorium; chemotherapy has on the average reduced the length of bed-rest. Nevertheless, many patients with more extensive disease still need prolonged treatment in sanatoria. These are now in many cases chest hospitals which have become active centres of treatment—as different from the old sanatorium as is the chest clinic from the old dispensary. The resources of thoracic surgery are often necessary; many patients are best removed for a time from the stress of a domestic environment, which may well have influenced the illness for the worse; for many others poor lodging or family troubles prevent domiciliary treatment. In a discussion on this theme at the meeting of the British Tuberculosis Association[6] sanatorium treatment still found its advocates, though many tuberculosis workers recognize the merits of the domiciliary treatment of tuberculosis wisely applied and with adequate resources. Most beds for tuberculosis have been provided in special hospitals, which have a fine record in training medical and nursing staff, and these beds are still needed if we are to ensure prompt admission of every patient. So our present "sanatorium" beds must still be used (though if new buildings for tuberculosis patients are necessary they would be better provided near to centres of population), but they should offer facilities not available to the home or clinic, as well as the basic routines of rest, graduated exercise, and chemotherapy which are common to all methods of treatment.

ENDOGENOUS DEPRESSION IN CHILDREN

Much attention has lately been paid to depressive disorders, especially the endogenous type. W. Mayer-Gross[1] at the B.M.A. Annual Meeting in 1954 described it as the commonest type of complaint in psychiatric patients to-day. General practitioners agree with the high incidence of the condition, and it is thought that about one-third of psychiatric patients suffer from depressive disorders. The classical endogenous depression is well known to all physicians, but over the past few years many minor variants have been added to the list. In 1953 Raymond Greene and Katharina Dalton[2] described premenstrual tension, which often assumes the features of a short recurrent depressive illness. J. Malleson[3] bore out their contention and described patients who became psychotic to the point of suicide. Early this year A. B. Hegarty[4] described a variety of post-puerperal depression which he concluded "is a common and important condition and it is at present insufficiently recognized." Now J. D. Campbell[5] discusses manic-depressive disease in children. His paper is descriptive rather than statistical, but he claims to have seen a large number of such cases and so long ago as 1952 published the records of 18 patients. Mayer-Gross *et al.*[6] state that, although manic or depressive psychoses do not as a rule make their appearance before adolescence, occasional cases have been observed. The suicide rate under the age of 9 is negligible. From 9–12 years the figures over the past 50 years are only 2–4 per million, but thereafter the incidence rises steeply. The fact that children commit suicide suggests that endogenous depression may occur as a rare disease in late childhood or early adolescence.

According to Campbell this type of disease can be diagnosed only by observing the patient over a long period of time and by studying the family as a whole, since there is usually more than one case of the disease in the family. This suggests that the disease in childhood is premonitory rather than fully developed. The melancholy child is usually a likable person who gets on well with his teachers and fellows at school. He tends to be a leader and he prefers organization and social and literary activities to sport. He forms a good rapport with his physician. This point is important, for in so many psychiatric conditions affecting children the patient keeps his doctor at arm's length. A manic phase may be seen as well as a depressive, but it is the latter which attracts most attention. The child is tearful and depressed. Night fears are common and there are sleep difficulties. He does not want to go to school, because retardation makes work difficult for him, and remarks about his changed attitude and ability are too painful to be endured. He has feelings of unreality and often a morbid interest in death. In most cases the disease is mild and self-limiting but is liable to recur. Electroplexy is not advocated for the very young. These depressed children are sad and retarded, but they are rarely eccentric, delinquent, or negativistic. In fact they rarely present any of the usual behaviour problems for which children are commonly referred to a psychiatrist. The general practitioner may be called in because of the child's moods or for some collateral condition. The disease is thus more likely to be seen by the family doctor than by the consultant psychiatrist.

Endogenous depression is an insidious and polymorphous disease, often difficult to diagnose in adults. In children it is even more difficult to distinguish pathological from reactive depression. The exuberant spirits of the young can simulate the exaggerated activity of manic patients, and the child who is frustrated or deprived can plunge into the depths of despair. Only too often children cannot, dare not, or will not open up and give voice to their feelings in a process of psychocatharsis which is relatively simple in the adult. Campbell admits that circumstances of a sort are usually found to explain the low spirits, but he maintains that careful assessment will show such claims to be spurious, and that the depression is in fact endogenous. The fact that a manic-depressive psychosis is rarely diagnosed in Britain among children does not mean that it does not exist. Once attention has been drawn to any disease, it is always surprising how many cases come to notice. If endogenous depression of childhood is indeed as common as Campbell suggests, it is most likely to be found with increasing frequency by those general practitioners who are on the look-out for it, even though it has so far largely gone unrecognized.

[1] Mayer-Gross, W., *British Medical Journal*, 1954, **2**, 948.
[2] Greene, R., and Dalton, K., ibid., 1953, **1**, 1007.
[3] Malleson, J., *Lancet*, 1953, **2**, 158.
[4] Hegarty, A. B., *British Medical Journal*, 1955, **1**, 637.
[5] Campbell, J. D., *J. Amer. med. Ass.*, 1955, **158**, 154.
[6] Mayer-Gross, W., Slater, E., and Roth, M., *Clinical Psychiatry*, London, 1954.

RADIUM TREATMENT OF DEAFNESS IN CHILDREN

Few episodes of medical inquiry exemplify so cogently the importance of the statistical method in the evaluation of a remedy as that initiated in 1924 by the investigations of Crowe and his associates of the Johns Hopkins Hospital into the cure of deafness in children by irradiation of the nasopharynx. S. J. Crowe claimed that the treatment gave a high rate of improvement.[1] In addition, much was made of certain audiometric findings, which were said to show that high-tone deafness, usually attributed to a disorder of the perceptive elements, was frequently caused by Eustachian insufficiency and was indeed diagnostic of it. The results obtained by subsequent workers have varied. Some are encouraging; others, as for example those of N. Canfield and D. Sudarsky,[2] are equivocal, with an improvement rate of some 50%. Although the diversity of good and poor results might be attributed, in contradiction to Crowe's claims, to the operation of chance factors, the alternative cannot be excluded that they are due to the diversity of the clinical material. In other words, the results may be derived from suitable cases showing real improvement and unsuitable cases showing none. The statistical inadequacy of Crowe's original claims were early recognized, and two further reports from Crowe's department have gone far to remedy the defect.

For the first of these, published in 1950, we are indebted to S. R. Guild,[3] who took as his normal base line the audiometric changes in 259 white children, first examined at or about the age of 9 years. All were found to have normal hearing and were re-examined at the age of 16 years. None of the children were submitted to treatment by irradiation or otherwise, and at both examinations the audiometric findings were correlated with the nasopharyngoscopic appearances of the Eustachian orifices. One fact established by this investigation was the occurrence of a well-marked increase of acuity for the lower frequencies up to 1,024 cycles per second. This was clearly a physiological accompaniment of ageing, and could not, as previously, be attributed to radium therapy. Guild also made observations on a number of children with abnormal hearing treated with radium, and the results obtained in a small series of children with deafness for all frequencies seemed to suggest that radium therapy could benefit this class of case.

Guild's contribution has now been reinforced by a further comprehensive clinical and statistical study by J. E. Bordley and W. G. Hardy[4] from the same department. In the first stage of their work an otological and audiometric study was made of 5,000 Baltimore schoolchildren, white and coloured, with an average age of 8 years. Of these, 385, all with slight hearing defects, were selected for study and were re-examined regularly at six-month intervals for five years. 193 were treated with radium; 192, the control group, received no treatment. It was found, first, that radium reduced the amount of adenoids in the nasopharynx, though in this respect puberty itself also plays an important part. Secondly, an effect of radium (and not attributable to puberty) was to reduce lymphoid tissue round the Eustachian orifices. Thirdly, low-tone acuity notably improved both in the treated subjects and in the untreated control group. This confirmed the finding of Guild and his attribution of the improvement to a physiological process. Fourthly, acuity for high frequencies slightly improved in both groups of subjects. This confirmed Guild's view that high-tone deafness is unlikely to be caused by obstruction of the Eustachian tube by lymphoid tissue or to be improved by radium. Fifthly, these investigators noted real improvement from the radium—again in accordance with Guild's findings—in subjects with an all-frequency type of deafness probably caused by tympanic changes.

These two notable papers seem to justify the hope, so long deferred, that a method with such clearly defined advantages, both theoretical and practical, may now after all enter upon a period of intelligent and fruitful application. May it also be hoped that the sponsors of further investigations of this complex subject will accept as their base line the commendable standards, both clinical and statistical, which have been established by the contributions of Guild and his colleagues.

[1] Crowe, S. J., *Laryngoscope*, 1940, **50**, 658.
[2] Canfield, N., and Sudarsky, D., 1949, *Ann. Otol. (St. Louis)*, **58**, 957.
[3] Guild, S. R., *Trans. Amer. Acad. Ophthal. Otolaryng.*, 1950, **54**, 508.
[4] Bordley, J. E., and Hardy, W. G., *Acta otolaryng. (Stockh.)*, 1955, Suppl. 120.

CITRATE INTOXICATION

Symptoms ascribed to intoxication with citrate ion have been reported in adults who had received massive transfusions with stored citrated blood[1] and infants treated for erythroblastosis foetalis by replacement transfusion.[2–4] Citrate exerts its harmful effect partly by lowering the ionized calcium level of the body fluids, partly by acting as a cardiac poison.[5] As a result of its effect on ionized calcium it might be expected to cause tetany, and this has been reported in infants,[2 3] occasionally with dramatically fatal results.[6] Ringer showed that the frog's heart could not beat in the absence of ionized calcium.[7] The depressant action of citrate on the heart is further illustrated by experiments on dogs in which the conditions of cardiac operations were simulated.[8] J. P. Bunker *et al.*[1] reported episodes of hypotension in some of their patients, and in three of them the hypotension was accompanied by "spectacular elevations of citrate" in the serum. Although Stefanini[9] found that there was a well-marked prolongation of the blood-clotting time *in vitro* when the ionized calcium fell to 0.5 mMol* per litre, Bunker *et al.*[1] were

[1] Bunker, J. P., *et al.*, *J. Amer. med. Ass.*, 1955, **157**, 1361.
[2] Wexler, I. B., *et al.*, *J. clin. Invest.*, 1949, **28**, 474.
[3] Ames, R., *et al.*, *Paediatrics*, 1950, **6**, 361.
[4] Smith, H., *British Medical Journal*, 1955, **1**, 1089.
[5] Love, G. R., *J. Lab. clin. Med.*, 1923, **9**, 175.
[6] Mellone, O., and Yahn, O., *Arch. Cirurg. clin. exp.*, 1949, **12**, 369.
[7] Ringer, S., *J. Physiol.*, 1883–4, **4**, 29.
[8] Cookson, B. A., *et al.*, *Ann. Surg.*, 1954, **139**, 430.
[9] Stefanini, M., *Acta med. scand.*, 1950, **138**, 250.
[10] Lazard-Kolodny, S., and Mayer, A., *Physicochim. biol.*, 1938, **14**, 265.
[11] MacKay, E. M., *et al.*, *J. biol. Chem.*, 1940, **133**, 59.
[12] Sjöstrom, P., *Acta chir. scand.*, 1937, Suppl. 49.
[13] Stoppani, A. O. M., *Medicina, B. Aires*, 1946, **6**, 389.
[14] Natelson, S., *et al.*, *J. biol. Chem.*, 1947, **170**, 597.
[15] Perske, H., *et al.*, *J. Pharmacol.*, 1950, **100**, 273.
[16] Report of the Council on Pharmacy and Chemistry, *J. Amer. med. Ass.*, 1951, **147**, 658.
[17] Melrose, D. G., and Wilson, A. O., *Lancet*, 1953, **1**, 1266.

* 1 mMol = one-thousandth of the molecular weight in grammes.

unable to correlate the raised clotting-time with low level of ionized calcium in the serum in 3 of their 14 patients.

Treatment of established or incipient citrate intoxication is by injection of calcium chloride or calcium gluconate, but it is difficult to calculate the dose required, and too much is dangerous.[1] Nor does treatment seem to be invariably successful in altering the ionized calcium concentration of the serum[4]; indeed, the serum citrate concentration increases after injection of calcium gluconate.[2]

Citrate is metabolized in the liver[10–12] and the muscles,[13] and is excreted and concentrated in the urine by the kidneys.[14] Therefore citrated blood is contraindicated for patients with moderate or severe hepatic or renal impairment. Anaesthesia with barbiturates[15] and possibly hypothermia[1] depress the activity of the Krebs cycle, upon which the metabolism of citrate depends. Several substitutes for citrated blood are available. Heparinized blood has the disadvantage that it may cause post-operative oozing of blood from the operation site. B. A. Cookson *et al.*[8] recommended the use of oxygenated red cells suspended in Ringer–Locke–gelatin solution, but gelatin is quickly eliminated from the circulation, and should not be given if renal function is impaired.[16] D. G. Melrose and A. O. Wilson suggested transfusion red cells suspended in salt-free dextran.[17] Bunker *et al.*[1] concluded that blood from which calcium had been removed by passage over an ion-exchange resin was the ideal material for blood transfusion when citrated blood is contraindicated. The disadvantage of all these substitutes is the complicated method of their preparation, and further work is necessary not only to find some simply prepared medium in which red cells can be transfused, but also to define precisely the mechanism by which citrate exerts its effects and the best treatment for citrate intoxication once it has occurred.

HYPERGLYCAEMIA AND VISUAL DISTURBANCES

It has been known for very many years that transient disturbances of vision are by no means uncommon in diabetics. These disturbances are not related to, nor are they manifestations of, diabetic retinopathy, the haemorrhages, exudates, and retinitis proliferans of which have so far proved resistant to all forms of treatment. Diabetic retinopathy, in so far as it may be delayed (but almost certainly not prevented) only by the most rigorous clinical control of the diabetes, is not simply related to instability of the blood sugar concentration, but is a manifestation of some more fundamental metabolic disorder. These transient visual disturbances, however, do appear to show a simple correlation with the amount of sugar in the blood. It is well known that hyperglycaemia, particularly in young subjects, tends to be associated with myopia, while a fall in the blood sugar concentration, either during treatment or with an overdosage of insulin, is often accompanied by hypermetropia and difficulties with accommodation. The explanation of these changes was discussed some thirty years ago.[1] It is also well known that, again especially in the young, prolonged hyperglycaemia is apt to lead to cataract formation, and that the cataractous changes in the early stages are typical in appearance and are reversible, in that they may disappear completely when the diabetes is brought under strict control. True diabetic cataract, starting with opacification of the lens cortex, occurs only, or predominantly, in the young, but in this connexion some recent observations are not without interest. In 1952 D. W. Vere[2] noted variations in the brightness of the ophthalmoscopic red reflex in normal and diabetic subjects which could be related to alterations in the level of blood dextrose. In a more recent communication he and D. Verel[3] have confirmed these observations and shown that the changes occur equally in young and old. Myopia induced in the experimental subject by persuading him to accommodate is associated with brightening of the red reflex, while hyperglycaemia leads to its dimming. The observed alterations in the brightness of the red reflex therefore run counter to those which might have been expected purely from refractive changes, and the authors have shown that they are due to reversible opacification of the deeper layers of the cortex of the lens. The nature of the underlying biochemical disturbance in the lens is not known. Whether or not alterations in refraction are associated with these lens changes, whether or not they are the precursor of true diabetic cataracts, and, if they are, why, in the older subjects, the changes do not more frequently progress are further questions which remain to be resolved.

VISIT OF RUSSIAN DOCTORS

The news of the visit of the six Russian doctors to this country in October has aroused much interest and has stimulated Dr. L. Crome to write a letter (see p. 438) to which brief reference might be made. At the time of the visit in December last year of twelve Russian doctors under the auspices of the Society for Cultural Relations with the U.S.S.R., the British Medical Association was one of many organizations which helped to entertain them. "When to do this was less popular than now," the B.M.A. three years ago invited Russia to send a delegation of doctors to this country, and now that it has fortunately become easier for Russians to accept such invitations they are coming, coming as medical men interested in the work of their professional colleagues in the United Kingdom. We are happy to be able to state that the Soviet Relations Committee of the British Council is co-operating with the Association, financially and otherwise, in providing our Russian guests with every opportunity for getting to know something of medicine in Britain and something, too, of the British way of life.

[1] Duke-Elder, W. S., *Brit. J. Ophthal.*, 1925, **9**, 167.
[2] *Lancet*, 1952, **2**, 1017.
[3] *Clin. Sci.*, 1955, **14**, 183.

EMERGENCIES IN GENERAL PRACTICE

ACUTE ALCOHOLIC POISONING

BY

J. A. IMRIE, M.D., F.R.C.S.Ed.

Chief Medical Officer, City of Glasgow Police

Cases of mild or medium intoxication are chiefly of medico-legal interest. The more severe states of intoxication are clinical emergencies presenting themselves to the general practitioner, the hospital casualty staff, and the police surgeon. The individuals concerned are peculiarly liable to a variety of complications, including falls, traffic accidents, suffocation by a variety of causes, drowning, exposure, carbon monoxide poisoning, and electrocution. The subjects of cardiovascular disease may precipitate acute cardiac failure by a debauch, and post-alcoholic debility may be complicated by acute pulmonary infections. In the suffocation group, inhalation of vomitus or respiratory obstruction by the tongue or dentures is not infrequent.

Dangerous Complicating Factors

The use and abuse of the barbiturate drugs have added a serious complication. It is generally recognized that a synergism exists between alcohol and the barbiturates, the latter being potentiated so that their anaesthetic and lethal levels are lowered if alcohol is present in the blood and tissues in adequate quantity. This potentiation can be fatal with concentrations of both drugs far below their ordinary fatal levels—for example, in one fatal case the blood alcohol indicated a minimum intake of the equivalent of three and a half large whiskies and a blood barbiturate level equivalent to taking 9 gr. (0.6 g.) of quinalbarbitone sodium. In such cases death can occur within a few hours. There is evidence also that morphine, or morphine–scopolamine, injected in therapeutic doses in persons with blood alcohols over 0.18% (180 mg./100 ml.) may cause severe morphine poisoning and perhaps death. Such cases have occurred when morphine was given to control violent alcoholics. Acute and chronic alcoholics are notably bad anaesthetic risks.

The combination of psychopathic personality with alcoholic intoxication may produce a clinical state out of all proportion to the amount of alcohol taken. *Mania a potu* may develop in those who have suffered previous cerebral trauma, or in the presence of epilepsy, cerebral arteriosclerosis, or unstable mentalities; even small amounts may produce a violent intoxication, greater than the same dose would cause in normal people. A more dangerous state arises in cases of chronic alcoholism where, either as a result of a short intense orgy or a more prolonged one or the sudden withdrawal of alcohol, delirium tremens or an acute hallucinosis develops.

Alcoholic Content of Various Liquors

The active principle of the common alcoholic beverages is ethyl alcohol. The distilled liquors—whisky, gin, rum, brandy, etc.—contain between 40 and 60% ethyl alcohol by volume. Wines vary from 10 to 20%, the fortified ones being the more potent. Fermented liquors—for example, beer and stout—vary, but the average content is 3–4% by volume. Sometimes methylated spirits is taken. This consists of ethyl and methyl alcohol in the proportion of 19:1, with certain impurities. The addition of a cheap red wine or other flavouring agent is common practice. This makes a potent mixture.

Clinical Progress

The dangerous states of intoxication are reached when there is gross locomotor incoordination and dulling of the intellect, with impaired judgment, and when coma develops. The time taken to reach these states and the severity of the symptoms depend on individual susceptibility, habituation, the amount of drink taken, the concentration of the alcohol, the speed of ingestion, and the presence of circumstances promoting absorption—for example, fasting—or liable to enhance the effect—for example, fatigue. Usually the clinical condition progresses by obvious stages, but occasionally the advanced states, even coma, may be reached very quickly and without preceding signs of intoxication. *Mania a potu* may be very early in onset, and epileptics are specially liable to become quickly intoxicated.

Clinically the distinctive symptom of these states is the vinous odour from the breath. This is usually not masked by deodorants in the severe cases and is to be distinguished from the smell of fresh alcohol recently taken, or perhaps given therapeutically by some good Samaritan in non-alcoholic conditions.

The well-known symptoms of moderate intoxication proceed to gross incoordination and inarticulateness, and the power of locomotion may be lost. At this stage vomiting may occur without affecting the progress of the intoxication but involving the risk of asphyxia. Unconsciousness develops; the face is usually flushed, the pulse rapid, and the blood pressure lowered; breathing is heavy and stertorous, and the temperature subnormal. The condition of the pupils is variable: they may be dilated, reacting sluggishly to light; or contracted, when they may show Macewen's sign. This is the dilatation of the pupil which occurs with shaking or slapping the patient without his regaining consciousness; when the stimulus is withdrawn the pupil slowly returns to the contracted state. This sign is strong evidence in favour of alcoholic coma.

As coma supervenes and deepens, muscular relaxation becomes complete and the face may become pale and sweaty, the pupils being contracted or dilated and fixed, the pulse rapid and of low tension, and the temperature subnormal. The duration of coma varies. In unaided recovery it gradually lightens into a deep sleep with improvement in all the symptoms and in the patient's condition. Coma persisting beyond five hours is of very serious moment, and apt to be fatal. Death from respiratory paralysis is likely if it persists for 12 hours.

Delirium tremens is one of the acute confusional states occurring in chronic alcoholics after a prolonged or a short intensive bout of drinking, or as a result of the sudden withdrawal of alcohol. It lasts for about three to five days, during which period there is a definite risk of death from cardiac or renal failure or an acute pulmonary infection. In the majority of cases recovery is to be expected. The distinctive feature of this form of delirium as compared with other delirious states is the generalized coarse tremor of the face, tongue, and hands, associated with prostration, tachycardia, lowered blood pressure, and a dry, furred tongue. Epileptiform convulsions and visual hallucinations are common, usually of small fast-moving objects like rats or insects. Intervals of apparent lucidity may occur with persisting disorientation for time and events. The mood varies, there being sometimes fear amounting to terror, excitement with violence, or these may alternate with jocularity. Restlessness and insomnia are prominent.

Differential Diagnosis

Alcoholic and other forms of coma have many features in common.* Comatose patients should not be left in police cells or unattended, and it may be fatal to assume that the smell of alcohol establishes the diagnosis. The diagnosis presents many difficulties, the chief being the association of head injury with alcoholic intoxication. Whenever there is the history, or the presence, of a head injury, a comprehensive general examination with particular attention to the nervous system should be supplemented by an immediate radiological examination of the skull, which may establish the presence of fracture. An estimation of the blood alcohol will indicate the part played by alcohol, since levels of 400 mg./100 ml. (0.4%) and over are likely of themselves to cause coma, and levels over 700 mg./100 ml. (0.7%) to result in death.

In extradural haemorrhage, the history and the pupillary changes are important. If alcohol has been consumed and there is also a head injury, the persistence of coma despite adequate treatment for intoxication, or initial recovery with treatment followed by recurrence of the coma, points to the probability of an intracranial lesion. Alcoholic coma may simulate pontine haemorrhage, but hyperpyrexia is absent. Other cerebral vascular conditions may be suspected if there is valvular heart disease or hypertension.

Coal-gas poisoning produces a red colour in the mucosae and cheeks, and the distinctive odour of the gas may be present. Death may occur with less than the usual lethal dose of carbon monoxide if alcohol is present in the body in sufficient concentration.

Coma due to barbiturates can usually be differentiated by the history and by the finding of congestion and cyanosis, shallow respiration, and signs of pulmonary oedema. When alcohol has also been taken barbiturate poisoning may be overlooked. If no history is available, a search of the clothing may reveal the drug or the empty container. Coma due to morphine or belladonna has characteristic features, though alcohol in moderate amount will potentiate morphine. In diabetic or hypoglycaemic coma the absence of the smell of alcohol should help to avoid confusion.

Treatment of Severe Intoxication

Once the diagnosis is established, treatment should aim at detoxication. Full recovery is not essential: recovery of consciousness, or at least a state of sleep, is adequate. Until then the patient should be under constant observation. Once he is detoxicated adequately he may be left to complete his own recovery. Since he will in all probability have passed his peak blood level by the time he is seen, it is doubtful if gastric lavage will be of material benefit. But if the patient is seen early, lavage can be undertaken, using a weak sodium bicarbonate solution and leaving 5–10 oz. (140–280 ml.) in the stomach. Continuous oxygen, in the form of a 90% mixture with carbon dioxide by mask or nasal tube, is recommended; it will allay excitement and cut short coma. Vitamin therapy has become popular and produces some startling results. Vitamin B_6 (pyridoxine hydrochloride) may be given in doses of 50–100 mg. intravenously, but if one injection fails to cut short the coma it is hardly worth repeating the treatment. More intensive therapy consists in the intravenous administration of vitamin B_1, 1,000 mg., vitamin B_6, 200 mg., and vitamin C, 1,500 mg. This is particularly applicable after prolonged bouts of drinking, when delirium tremens is impending.

Nikethamide, intravenously or intramuscularly, has been in use for many years. It is usually given intravenously and is rapidly inactivated after injection. Doses of between 5 and 10 ml. have been given with striking results. When more than 3 ml. is given, the injection should be made slowly and a careful watch kept for muscular twitchings to avoid the production of convulsions. The drug should be administered only by the doctor in attendance. Recovery is often rapid, and is ushered in by sneezing or vomiting or both. The best results seem to be obtained in the young and non-habituated. In the older, more habituated group a combination of vitamin B_6 and nikethamide in smaller doses may be effective. These forms of treatment have been found to allay excitement. Caffeine and sodium benzoate *B.P.*, 1 g., intravenously is stated to be beneficial in both the comatose and the excited such as those with *mania a potu*. In these latter cases the forms of intravenous therapy described are often successful and obviate sedation.

Delirium Tremens

Delirium tremens requires the sedation of the patient and the correction of the nutritional deficiency. Home treatment involves much strain on the attendants. Hospitalization is more appropriately carried out in general hospitals, certification being undesirable unless there is also alcoholic dementia. Cases of alcoholic dementia are appropriately admitted to mental hospitals.

Morphine, morphine with hyoscine, and paraldehyde are unsafe in delirium tremens. Nor is the use of barbiturates without danger if alcohol is present in the blood and tissues. Detoxication with vitamins B_1, B_6, and C intravenously in the doses already indicated is particularly suitable for these cases. This treatment may be repeated daily in rather smaller dosage. A rapid abatement of the nervous symptoms is to be looked for, and from a nutritional point of view the vitamins are essential. Sedation may be unnecessary with this treatment. Alternatively, if there is no barbiturate–alcohol risk and sedation is necessary, a quick-acting barbiturate, in full dose, can be given by mouth, followed by a slow-acting one. If oral administration is impossible, an initial dose of phenobarbitone sodium, 3 gr. (0.2 g.), can be given intramuscularly.

Gastric lavage with weak sodium bicarbonate is a useful preliminary to tube feeding, should this prove necessary. If nourishment cannot be given by mouth a tube feed of 10–15 oz. (280–420 ml.), containing glucose, 3 oz. (93 g.), hydrolysed protein, 1 oz. (31 g.), with 300 mg. of ascorbic acid and vitamin B complex, is given four-hourly. The amount of fluid is gradually increased. When the delirium abates and the patient can swallow, fluid with high carbohydrate content is given by mouth. The administration of brandy or whisky (up to 1 oz. (28 ml.) and repeated four-hourly till delirium subsides) in cases with extreme weakness is a question for the attending physician. The use of corticotrophin (A.C.T.H.) in 25-mg. doses intramuscularly every six hours is stated to have encouraging results during the acute stage of the delirium.

Once the delirium is over and nourishment is being taken adequately, treatment consists in improving the general health.

Methyl Alcohol Poisoning

Poisoning by methyl alcohol is uncommon and usually occurs in minor outbreaks, but individual cases do occur and may be missed.

Methyl alcohol is used commercially as a solvent for paints, varnishes, and shellacs, and is present in some anti-freeze mixtures. Sometimes alcoholic beverages—for example, whisky—are adulterated with methyl alcohol. Many of the fatalities from alcohol during prohibition in America were due to this alcohol. It is one of the constituents of methylated spirits. The sale of methyl alcohol is controlled by the Customs and Excise.

The response to methyl alcohol is variable. Large amounts—for example, 500 ml.—have been drunk without death resulting, while 15 ml. of 40% methyl alcohol has caused death. It gives the same symptoms of intoxication as ethyl alcohol. The symptoms of poisoning do not appear until after a latent period of 15–24 hours, or occasionally longer (up to 40 hours). Rarely they develop within an hour or two. During this latent period a condition of acidosis develops,

*See also article in this series by Dr. M. J. Parsonage on "The Differential Diagnosis of Coma" (January 22, p. 217).

the result of the oxidation of methyl alcohol to formic acid and formaldehyde. The plasma-bicarbonate level is lowered and the prognosis can, in fact, be measured in terms of the plasma-bicarbonate level, death being likely when this is below 10 mEq per litre.

When poisoning occurs it is ushered in by headache, usually severe, nausea, giddiness, and epigastric pain. Accompanying these there are visual symptoms, usually blurring of vision. At this stage retinal changes may be evident, with hyperaemia of the optic disk and oedema of the adjacent retina. Cyanosis and dyspnoea develop, and coma sets in early. The skin is cold and clammy and there is tachycardia. The pupils are often dilated and show sluggish reactions. Prostration is severe, and finally there is respiratory failure and death. The coma may last for several days. The ocular changes may occur early or may follow recovery. Photophobia and blurred vision, or even complete blindness, may occur within 12–24 hours.

The combination of gastro-intestinal and visual symptoms following a latent period after drinking alcohol should suggest methyl alcohol poisoning, and direct attention to the plasma-bicarbonate level if facilities exist for its estimation. The fact that others who indulged in the same drinking bout are not affected does not exclude methyl alcohol, since it is recognized that if ethyl and methyl alcohol are taken together there may be considerable variation in the individual responses.

Treatment of Methyl Alcohol Poisoning

Treatment is aimed at combating the acidosis. When intense shock is present with signs of respiratory paralysis intravenous nikethamide, 2–5 ml., can be given. Continuous oxygen is also indicated, but gastric lavage is useless, if not actually dangerous.

Alkalis should be given at once by the intravenous route. Sodium lactate, a molar solution (11.2%) in an isotonic solution of the three chlorides, gives excellent results. Injectio sodii lactatis co., *B.P.*, can be given. If sodium lactate is used in molar solution, the injection should not be given more rapidly than at a rate of 300 ml. an hour. The dosage and frequency of the injections are determined by the severity of the symptoms and the results of repeated estimation of the plasma-bicarbonate level. The more severe the symptoms, the higher the initial dose. If there are no facilities for plasma-bicarbonate estimation, the *p*H of the urine is a satisfactory guide, or its reaction to litmus paper. When the urine becomes alkaline, there is a danger of tetany, hypokalaemia, or sodium retention, and the administration of alkali should be stopped and resumed only if the symptoms of poisoning recur or the urine turns acid again.

Alternatively, sodium bicarbonate intravenously provides a simple and safe method if similar controls are observed. A solution of 50 g. of sodium bicarbonate in 1 litre of 5% glucose is given, the amount administered being determined by the severity of the initial symptoms, and thereafter by the plasma-bicarbonate level or the *p*H of the urine. If intravenous administration is not immediately possible and the patient can take the bicarbonate by mouth or by stomach tube, doses of 4 g. are given every 15 minutes if they can be tolerated. In all cases careful control of the plasma-bicarbonate level or the urinary *p*H should indicate the amounts required.

Other Alcohols

Of the remaining alcohols, propyl and isopropyl alcohol have an action similar to ethyl alcohol but are more toxic. They are used industrially in the manufacture of perfumes, toilet articles, and certain lacquers. They are much less volatile than other alcohols and are uncommon as poisoning agents. Ethylene glycol is used in the manufacture of antifreeze mixture. On occasions it has been known to cause death accidentally and has been used suicidally.

Next article on Emergencies in General Practice.—"Is It Polio?" by Dr. T. Anderson.

UGANDA AND GREAT ORMOND STREET

AN EXPERIMENT IN GLOBAL PAEDIATRICS

BY

BERNARD SCHLESINGER, O.B.E., M.D., F.R.C.P.

Senior Physician, Hospital for Sick Children, Great Ormond Street, and to the Children's Department, University College Hospital

One of the most recent activities of the Hospital for Sick Children, Great Ormond Street, is a liaison with the paediatric services of Uganda, hitherto very scantily provided. A senior registrar from Great Ormond Street has been seconded to the Protectorate for a two-year period, and he will be followed in turn by further registrars. In addition two nursing sisters from the hospital volunteer to go out and take charge of the children's wards for a similar period, and each year one of the Great Ormond Street consultants will pay a month's visit.

Among the reasons that have led to this new venture is the desire to keep abreast of the rapidly increasing global

Children's ward, Mulago Hospital, Kampala.

nature of medicine brought about by modern air travel, better knowledge of tropical paediatrics being particularly important. Many postgraduates from the Orient attend the courses of the Institute of Child Health at Great Ormond Street, and it was realized that the special problems they would encounter on their return were not being adequately covered. There was also the pressing need for improved care of the vast number of sick children in Africa and the introduction of up-to-date methods. When it became known that the Uganda medical authorities would value such help, with the aid and financial assistance of the Colonial Office, the co-operation of Makerere College at Kampala, and the generosity of the Board of Governors of the Hospital for Sick Children, Great Ormond Street, the Uganda scheme was promoted.

So far the liaison has worked admirably. It has proved of great benefit to the Mulago Hospital, through the teaching and example set by the small band from Great Ormond Street. Equally, the experience gained by the doctors and nursing sisters from London has been invaluable in widening their horizon, taxing their ingenuity, and increasing their responsibility. Disease is encountered in a raw and florid state undreamt of in England, and offers the young doctor and research worker innumerable problems to solve. The team from Great Ormond Street has been welcomed and wholeheartedly supported. The registrar occupies a privileged position, acting virtually as aide-de-camp to Dr. HUGH TROWELL, a general physician who has taken paediatrics as an additional specialty under his wing.

The nursing sister has a difficult task in controlling her overcrowded ward, the African nurses, and the mothers, who invariably accompany their children into hospital (see Fig.). In face of numerous frustrations she has introduced many advances in nursing and the special techniques involved in the treatment of sick children. The addition of a second Great Ormond Street sister to the staff will go a long way in overcoming several of her difficulties.[1]

The unique position of Uganda in Britain's colonial enterprise is an added incentive to the scheme and augurs well for the future. Anyone who travels in Uganda cannot help being fascinated by the country and by the enthusiasm of the doctors who are working there. This has such a strong appeal that no visitor can leave without a most vivid and memorable impression: anyone with ideas, sympathy for the people of Africa, and a pioneer spirit must feel happy and satisfied with the work. Not a little of this contentment is due to the general atmosphere of co-operation and hospitality that exists among the doctors, which soon makes a newcomer feel at home. The liaison begun by the Hospital for Sick Children, Great Ormond Street, is undoubtedly worth while, and it could profitably be extended to other parts of the Empire in branches of medicine beyond paediatrics. There can be no better way in fostering Anglo-African relationships. "Pain makes of all people one tribe."[2]

THE ROLE OF THE MIDWIFE, THE FAMILY PRACTITIONER, AND THE SPECIALIST IN NORMAL LABOUR

[FROM A SPECIAL CORRESPONDENT]

At the fourteenth British Congress of Obstetrics and Gynaecology, held at Oxford from July 27 to 30, the third morning was devoted to a discussion on the role of the midwife, the family practitioner, and the specialist in normal labour.

Maternity Services in America

The first speaker, Professor JOHN L. MCKELVEY (Minneapolis, U.S.A.), opened disarmingly by saying that he had had little experience with midwives, for they had almost disappeared from the obstetric scene in the United States and Canada, and that he could not predict which woman would and which would not have a normal labour. In his country both the general public and the medical profession were in accord with the policy of confining maternity services to well-equipped institutions with highly qualified staffs. The conception of the general practitioner as a second-class citizen was absurd; their experience had proved that the family doctor who chose to practise obstetrics could be brought to a high degree of skill and sense of responsibility. Indeed, in America most of the obstetrics was conducted by family doctors. They were able to do this because they had access to their local hospitals with all the attendant facilities, including close contact with the more experienced specialists.

The Midwife in Britain

Mr. ARNOLD WALKER (London), chairman of the Central Midwives Board, dealt with the system in Britain as it was and as it might be improved. He said that about 60% of confinements occurred in hospitals, and that about 80% of all deliveries, inside and outside hospitals, were conducted by midwives. In urban areas the bulk of obstetrics undertaken by general practitioners was done by a small minority, but even these were present, much less conducted the delivery, at surprisingly few labours each year. Moreover, much antenatal care was given by family doctors who rarely saw a baby born, a criticism previously levelled at the staffs of local health authority clinics.

It seemed to him that the acceptance of special obstetric lists by the profession implied that midwifery was no longer regarded as an essential part of general practice. The corollary was there should be a strong midwife service, with a limited number of general practitioners handling enough obstetric cases to retain interest and efficiency. He advocated the appointment of such specially trained family doctors to permanent part-time hospital posts under the supervision of consultants, replacing the excessive number of registrars for all of whom eventual consultant status could not be envisaged. As for the midwife, her responsibilities must not be further curtailed. She was a valuable partner in the team, highly trained in the management of pregnancy, labour, and the puerperium, ever cognizant of when medical aid should be summoned, and in more intimate contact with the pregnant woman than the doctor could be. In summary, the present system was sound and it would be wasteful to spend medical manpower on replacing the midwife. It would be better to have a strong midwife service, with the eradication of the present weakness—the fact that too many general practitioners were competing for too little obstetrics.

The General-practitioner Obstetrician

Dr. G. F. ABERCROMBIE (London) presented the viewpoint of a family doctor practising obstetrics. He said that the role of the general practitioner was to be at a certain place at an uncertain time. At the confinement his job was to guarantee a happy outcome, and so he must plan that any complication could be successfully met either by his own efforts or by those of a specialist colleague. The general-practitioner obstetrician should be experienced and competent in external version, breech delivery, surgical induction of labour, manual rotation of the head, forceps extraction, manual removal of the placenta, and repair of cervical and perineal lacerations; but about 5% of his patients would require a procedure—for example, caesarean section or blood transfusion—which he could not personally undertake.

Most multigravidae, said Dr. Abercrombie, could be safely delivered at home, but every primigravida underwent in effect a trial labour. She should therefore be delivered in an institution where an anaesthetist, a theatre, and an extra pair of hands were provided, but she might be returned home for the puerperium if medical and social circumstances permitted. He therefore deplored that nowhere in London did the general practitioner have access to a hospital maternity unit, and he pleaded for the hospitals to open their doors to all patients and all doctors who sought entry.

Views of the Meeting

The subsequent general discussion was lively, but pressure of time, the lack of opportunity for the cut and thrust of debate, and the limited terms of reference of the subject may have prevented the meeting really coming to grips with the whole problem of a national maternity service. A stout defence of the midwife, as teacher as well as nurse and practitioner, came from all sides. Pleas were made for the greater training of the medical student in domiciliary obstetrics, and for the closer study by the specialist of the phenomena, physical and psychological, of normal labour. Perhaps the best impressions from the floor were made by the general-practitioner obstetricians who spoke, for they showed with facts and figures how co-operation with colleagues, midwives, and specialists could produce excellent results, provided that the general practitioner had access to maternity units. In this respect the rural practitioner seemed more fortunate than his colleague from the city, but it was interesting and encouraging to hear that in Oxford there was now a general-practitioner obstetric unit in a teaching hospital, accepting normal cases where domiciliary confinement was ruled out on social grounds.

In summary, the general feeling of the meeting seemed to be that, while there were defects in the present system,

[1] A fuller account of the scheme will be given in the next issue of the *Great Ormond Street Journal*.

[2] From Esther Warner's *Trial by Sasswood* (Gollancz, 1955).

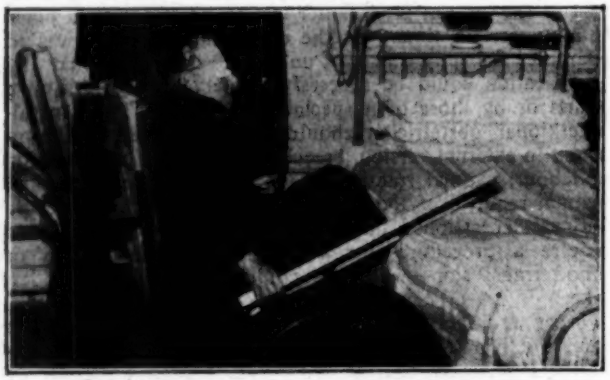
its virtues could be greatly enhanced by better organization, by closer co-operation, and, above all, by seeing that the general practitioner who chose to practise obstetrics handled enough material to maintain his skill and knowledge, and had access to all facilities, including a maternity unit.

Preparations and Appliances

AIDS FOR THE DISABLED: BRIDGING THE GAP FROM BED TO CHAIR

Mrs. KATHLEEN VINDEN, M.A.O.T., and Dr. J. R. D. BAYNE, of the geriatric unit, West Middlesex Hospital, write: One of the problems facing a rehabilitation unit is that of making the person with chronic rheumatoid arthritis independent. He must learn to dress, feed, and wash himself. If the knees and hips are already so severely contracted that he cannot walk, he should be trained to use a wheel-chair. He may, however, even with a low bed, find it impossible to stand only for a moment to get into and out of his wheel-chair without help.

In answer to this challenge, one of our patients suggested using a board as a bridge to slide along to the chair or back to the bed. A number of patients have now used this method, and we have modified the board to make it most suitable. It should be strong but light enough to be managed by crippled arthritic hands and narrow enough to be put under the buttocks with the patient in the chair. The illustrations show a patient aged 73, weight 9 st. (57 kg.), placing the board and sliding along it to the bed. One arm of the chair is removed for visibility—the patient does not remove it normally. The board consists of a piece of birch plywood, 30 by 7¼ in. (76 by 20 cm.), well sandpapered, polished, and mounted by panel pins to a frame made of deal wood ⅞ by ⅞ in. (2.2 by 2.2 cm.). Tenon joints and two centre battens are used to strengthen the frame. The weight is 1 lb. 13 oz. (0.8 kg.). For patients over 12 st. (76 kg.) a stronger frame is made from beech plywood surface and a pinewood frame. The approximate cost of the materials is 5s.



Nova et Vetera

SYDENHAM ON SMALLPOX

In 1667 Thomas Sydenham was practising in Pall Mall when John Locke arrived in the Metropolis as physician to Lord Ashley, afterwards the first Earl of Shaftesbury. Locke soon formed an acquaintance with Sydenham, whose novel treatment of fevers outlined in his *Methodus Curandi Febres* had recently been received with hostility among those physicians who valued subtle speculation more highly than careful observation based on diligent practice. Locke was quick to realize the merit of Sydenham's work, which he acclaimed in a long poem in Latin prefaced to the second edition of the book on fevers.

Their friendship soon blossomed into active collaboration: together they visited many patients stricken with smallpox, and they planned a joint treatise on it. "I perceive my friend Mr. Locke," writes Sydenham to Boyle in 1668, "hath troubled you with an account of my practice as he hath done himself in visiting with me very many of my variolous patients especially."[1] In Sydenham's name Locke wrote a dedication which clearly shows that Locke had called on Sydenham's greater experience in the treatment of smallpox occurring within the Ashley household. "At least, my lord, I thought it reasonable to let you see that I had practised nothing in your family but what I durst own and publish to the world, and let my countrymen see that I tell them nothing here but what I have already tried with no ill success on several in the family of one of the greatest and most eminent personages amongst them."[2]

Unfortunately the treatise was never completed; but the following notes (from the Locke manuscripts in the Bodleian Library) may have been intended as part of the work. They were written by Sydenham, who sent them to Locke for correction and possibly for translation into Latin. As Sydenham's works were first published in Latin, this note on smallpox, with its many alterations, is of interest in that it is one of the few examples of his original writing.[3]

Further observations of feavers.

Variola.

Since my writing the foregoing discourse of the smallpox I have further observed that in a flox pox ordered in my way the patient begins to spit about the 5th d., his face to begin to swell 6, to be bluid 7; and likewise that when the pustules are at their height those on the hands and legs are large, but growe less and less proportionally as they are placed nearer the truncke, those on the brest back and belly being very little which also about 14 d. are most gone when at the same time, those on the hands and legs stand up high full and of a white colour; about 16 or 18 d. the patients legs begin to swell which yet will sink again after purging.

I have likewise met with a sort of flox pox never before by me seen. They came forth about the 2nd d. with one general uniform red swelling all over the face, more like an erysepalas without the least distinction of any apparent pimples at all: in the other parts of the body pustules arise hereof many are very deep shining red something tending to purple, and besides those here and there

between them, especially upon the thighs, blisters, whereof some are as big as walnuts filled with their water, which breaking the skin runs out and leaves the flesh under it mortified. In the progress of the disease a white shining skin comes on upon the red swelling in severall parts of the face, in large patches of it had a tendency to spread all over, some parts of the face nevertheless left remaining still red. This white skin in a little while spews up a glasy inky matter, which is not as in the other sorts of small pox either yellow or russet, but of a deep red colour not unlike congealed dry blood, which every day grows darker till it comes at last to a perfect black. I have seen tryall both of hot and cold keeping in this species but neither of them have succeeded though yet I find by how much the colder they are kept by so much they are the securer from mortifications and I am apt to believe that bleeding joyned with moderate keeping will do well.

Written 14° Feb. $\frac{69^{*}}{70}$.

Keystone of Practice

Infectious diseases (particularly smallpox) were the keystone of seventeenth-century practice. Between 1667 and 1669 Sydenham studied epidemics of discrete and confluent smallpox: later he described anomalous and haemorrhagic or "flox smallpox." This account of haemorrhagic smallpox summarizes a more detailed description in a Bodleian manuscript entitled "Extracts of Sydenham's Physic Books and Some Good Letters on Various Subjects,"[4] which was published by Dr. W. E. Greenhill as *Anecdota Sydenhamiana* in the mistaken belief that they were written by Sydenham. Mr. Fox-Bourne and later Sir William Osler noted that these manuscripts had been written by Locke, who had copied them from Sydenham's rough drafts. They further demonstrate the close collaboration between these two Oxford physicians.

It is clear from the *Anecdota* that Sydenham found the "flox smallpox" the most difficult to treat until he instituted a "downright cooling regimen." He observed that while the patient was ambulant he was reasonably well; but on returning to bed "then presently came on ill symptoms of feaverishness Inquietude, yea and some degree of a Phrensy." Until Sydenham's writing became recognized variolous patients were treated with a so-called "hot" regimen. They were put to bed, kept well covered, and given stimulating cordials with a view to bringing out the disease. "By such means," writes Sydenham, "greater slaughters are committed and more havocke made of mankinde every yeare than hath bin made in any age by the sword of the fiercest and most bloody tyrant that the world ever produced."[5]

The principles of Sydenham's cooling method have been embodied in the modern symptomatic treatment of smallpox, for they were based on the astute observations of a clinician who limited himself to

> Knowing what's what and that's as high
> As metaphysic wit can fly.

KENNETH DEWHURST.

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2 P.R.O. File. 30/24/47/2.
3 MS Locke. C.29, folio 22.
4 MS Rawl. C.406.
5 Payne, J. F. (1900). *Thomas Sydenham*, p. 176.

*69 is the legal year 1669, and 70 the historical year 1670.

The University Hospital at Lille has a novel method of allowing students to participate in medical examinations without discomfort or embarrassment to the patients. This system is explained by John Dodd, in *French Hospitals and Health Services* (British Hospitals Contributory Schemes Association, Bristol, price 10s.). The students sit in an amphitheatre, seating 240, above a consulting-room where the patient is examined in private. Images of his lesions are projected to the amphitheatre for the students to see. Above this screen is another on which a lantern operator at the back of the hall can throw relevant diagrams. The lecturer's voice is also relayed from the consulting-room.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Treatment of Acute Leukaemia

SIR,—The paper by Dr. Ronald Bodley Scott on the treatment of acute leukaemia (*Journal*, July 9, p. 75) was of considerable interest and his remarks concerning the prognosis in adults are soberly correct. But are there no grounds for optimism when, to quote from his conclusion, "in some instances and for short spells, the leukaemic process can be checked or reversed"? The position in children is somewhat less depressing, and, as a result of observations that I have been privileged to make at the University and Philadelphia Children's Hospitals in the University of Pennsylvania, I am more ready to agree with his hope "that a means of controlling this tragic disease will one day be vouchsafed to us."

While the degree of success obtained in the larger centres, such as the Sloan Kettering Institute and Memorial Hospital in New York and at the Children's Cancer Research Institute in Boston, is greater than can be expected in most hospitals, the results in the University of Pennsylvania project are encouraging. No one working in this field would be so rash as to claim that anything more than a beginning has been made in the chemotherapy of malignant disease, but the clinical response provides good reason for intensifying research into these problems.

Fifty children with acute leukaemia have been treated in a sixteen-month period, of whom 66% have shown a significant clinical and haematological remission. In addition to the usual general care and blood transfusions that have been given, a combination of antimetabolites such as aminopterin, 6-mercaptopurine, and thioguanine, as well as corticotrophin, cortisone, or Δ^{14} dehydrocortisone (metacortandracin). The cost of their care and other basic research work has been met by a grant from the United States Public Health Service to the University of Pennsylvania under the direction of Professor Ralph Jones, jun. The average length of survival from onset of symptoms to death was 40.4 weeks in 36 cases, in contrast to 13 weeks in a comparable series of 22 cases seen in 1948 and 1949 before the use of antifolic compounds. The average length of the initial remission in 33 cases was 15.4 weeks. Second remissions were induced in 13 children (26% of all cases; 39% of those showing a previous remission) which lasted an average of 14 weeks. Surprisingly, third remissions have occurred in two children after resistance to one or more of the antimetabolites had developed. Since 14 children are still alive there is still room for improvement, but 10 have lived for one year or more after the onset of definite symptoms and five have lived for one year after diagnosis. Burchenal's[1] figure of 52% surviving for one year is considerably better, but our cases, as in many other series, have probably been less highly selected and several have had relatively ineffective experimental drugs.

Having at one time been sceptical about the wisdom and morality of treating these children, I am now convinced that such a course is right, not only from academic interest but also from the point of view of both children and parents. The minority in whom the response is excellent often return to vigorous activity, continue to grow, and show such little evidence of leukaemia that, were one not to know the history, a physical or bone marrow diagnosis would be impossible. Very often the perplexed parents are genuinely thankful that nothing has been left undone that might have benefited their own child or other unfortunate leukaemics. Although the antimetabolites and steroids at present available are of limited scope, they are nevertheless extremely potent drugs. How frustrating and tantalizing this is!

In spite of the tragedy which each individual case inevitably presents, I am sure that many will agree with my simple

optimism that within the next two decades some of these malignant diseases will be palliated as successfully as pernicious anaemia and diabetes—where, after all, a cure is still lacking.—I am, etc.,

Philadelphia. KENNETH GURLING.

REFERENCE

[1] Burchenal, J. H., *Cancer Res.*, 1954, **14**, 615.

Replacement Transfusion with Saline-suspended Red Cells

SIR,—In order to reduce the serum bilirubin level of a 6-day-old group B child presenting with increasing jaundice, but without anaemia, an exchange transfusion was performed. The possible diagnosis of haemolytic disease due to ABO incompatibility was supported by the presence of an anti-B haemolysin and the incomplete form of anti-B, both active at 37° C., in the group O maternal serum. For this reason, to reduce the complement and antibody content of the blood transfused, washed group O cells suspended in saline were used.

The exchange transfusion was carried out with no technical difficulty, 450 ml. of blood being exchanged in 70 minutes. Immediately following the transfusion, the child's condition steadily deteriorated and it died within one hour of the cessation of the transfusion. Electrocardiographic tracings showed sporadic normal complexes. The child's serum bilirubin at the commencement of the transfusion was 17.2 g.%, and at the end of transfusion 2.5 g.%. The potassium content was 19.2 mg.%, and after transfusion was still at the same level. The serum proteins at the commencement of transfusion were 6.3 g.%, and after transfusion 1.2 g.%. This child appeared to have died owing to inability to maintain its serum proteins, apparently as a result of hepatic insufficiency.

It would seem that newborn children and adults are able to maintain their serum proteins during a straightforward transfusion with cells suspended in saline, and a very limited experience of exchange transfusion of the newborn with saline-suspended cells has not previously caused concern. It would appear, however, that such a transfusion may be lethal in an infant with liver insufficiency.

We feel it necessary to draw attention to this child in order that others considering this form of transfusion in the newborn should be aware of its possible lethal consequences. Possibly re-suspension of the cells in pooled plasma would be a better procedure.—We are, etc.,

C. C. BOWLEY.
J. L. EMERY.
R. S. ILLINGWORTH.

Sheffield, 1.

A New Look at the Curriculum

SIR,—As the medical curriculum (*Journal*, July 16, p. 188) is something which affects students more closely than those who are already qualified, it is perhaps not unreasonable that a student should express his views. At the end of the report of the medical teaching committee of the Royal College of Physicians is an appendix which suggests reviewing each stage of the curriculum, and it is on this that I would like to enlarge.

The premedical period.—At the moment an examination in physics, chemistry, and biology is taken as a preliminary to the rest of the course. I heartily agree with the report which states that the amount of specialized knowledge required in the basic subjects of physics, chemistry, and biology should be restricted so as to make possible a broader general and cultural education. Is it possible that the first M.B. examination in some universities is now nothing more than an eliminating process which renders the job of a selection committee less difficult? The following suggestion could perhaps be entertained: make it compulsory to take the first M.B. examination at the university; but also point out to the candidates that it is not necessary to have any knowledge of physics, chemistry, and biology beyond the level of the General Certificate of Education. The course would be simpler and would be kept as far as possible to things which could be applied to medical work. This would be quite adequate as a scientific background for the medical course.

The preclinical period.—It would help considerably if the physiology and anatomy departments could be blended more closely together. If this were done, then one would not find oneself dissecting the brain in the Easter term, having anatomy lectures on the brain in the summer, and physiology lectures on the central nervous system at some other time.

The clinical period.—It seems that far too much time is spent learning pathology as a separate subject. I have been doing this for two and a half years (normally a degree course lasts three years). Perhaps one year doing general pathology would be enough while the more specialized parts of the subject could be taught by the clinical teachers of medicine, surgery, and midwifery. Pharmacology tends to be taught apart from rather than in the wards. As the subject widens so the pharmacologist becomes more of a scientist and less of a doctor.

Lastly, since the vast majority of students are going into general practice, it seems extraordinary that so little is done to give one any indication of the problems and workings of general practice. One can stand on ward rounds listening to a deposition on some rare disease, or watch patients undergoing weird and complicated tests, and wonder how much one's own family doctor knows or ever knew about such things. A little more teaching by general practitioners and a little less from specialized teachers might do some good.—I am, etc.,

Bristol JOHN STEPHEN.

Tonsillectomy

SIR,—I have read the article by Mr. J. C. Campbell and Dr. D. Hunter Smith (*Journal*, June 18, p. 1451) and the subsequent correspondence with great interest. May I congratulate the authors on an excellent paper? Their record of over 12,000 cases without a death must surely speak for itself.

Many of the objections raised against the guillotine operation are invalid, and I always suspected that some of those who protest must have never learned to master the technique. With all respect to Mr. James Crooks (*Journal*, July 2, p. 58), I can assure him that a perfect and unhurried adenoidectomy need take no longer than 15 to 20 seconds. Having said this, I must sound a note of warning, especially to those of my young colleagues who, like myself, learned their guillotining in teaching and specialist hospitals, where this was the standard procedure. Mr. S. R. Mawson and Dr. F. F. Cartwright (*Journal*, July 9, p. 139) have already stated their reasons for abandoning the guillotine method. Their objections are based chiefly on the difficulties of adequate premedication, timing of anaesthesia to coincide with a quick yet unhurried operation (especially removal of adenoids), and the "uncontrolled" bleeding. I thoroughly agree with them and with Mr. Campbell and Dr. Hunter on the need for the expert anaesthetist. But I would go further and say that the whole "team" of surgeon, anaesthetist, *and nursing staff* must be guillotine experts.

Under the conditions prevailing in most regional board hospitals there are frequent changes of theatre sisters, student nurses, orderlies, and even anaesthetists. Under those circumstances it becomes wellnigh impossible to have a trained team. It is this which is to me the greatest obstacle in continuing the guillotine operation, and I suspect many E.N.T. surgeons have given it up for similar reasons.—I am, etc.,

Chislehurst. E. H. RAINER.

SIR,—Dr. Arthur Tom (*Journal*, July 16, p. 201) is to be congratulated on his courage in advocating the use of thiopentone for guillotine tonsillectomy in children, an anaesthetic technique that I have found inevitably occasions criticism from those unacquainted with the method. In 1953, in an attempt to produce better operating conditions

for the more inexperienced juniors, I investigated the use of thiopentone as a sole agent for this procedure, and soon adopted the method for all occasions. Critical and close observations of the effects of this drug, now used routinely for nearly three years, have proved the technique to be sound and safe, the operative conditions to be uniformly ideal, and the theoretical disadvantages to be absent in practice.

However, I fear that, while Dr. Tom states that his dose (0.05 g. per year, minus 0.05 g.) is a rough guide and varied according to the general type and size of the child, he fails to stress sufficiently this most important part of the procedure. The plea that dosage of drugs should, as a general principle, be based on body weight and not age has been raised before, and I make no apology for raising it once more. With some drugs less specific administration is permissible, but with thiopentone it has been shown that dosage can be related to body weight, particularly fat. In the very young (where the variations in body weight and fat are great, even in similarly aged children, and may range as much as 50% on either side of the generally accepted "average") my own experience leads me to believe that for consistent and reliably safe results a dosage based on body weight is necessary. This involves neither great hardship nor mathematical strain.

In the last 207 children admitted for tonsillectomy I have examined the weight to age relationship, which underlines the unreliability of the latter to serve as a basis for drug administration.

Weight to Age Relationship in 207 Tonsillectomy Cases

	2 Years	3 Years	4 Years	5 Years	6 Years	7 Years	8 Years	9 Years	10 Years
25 lb. (11·3 kg.) ..	—	2	—	—	—	—	—	—	—
30 „ (13·6 „) ..	1	2	4	4	2	—	—	—	—
35 „ (15·8 „) ..	—	1	5	15	7	2	2	—	—
40 „ (18·2 „) ..	—	—	2	8	22	17	1	—	—
45 „ (20·5 „) ..	—	—	—	5	14	15	7	1	—
50 „ (22·7 „) ..	—	—	1	2	7	10	6	3	—
55 „ (24·9 „) ..	—	—	—	—	2	6	7	4	—
60 „ (27·2 „) ..	—	—	—	1	—	2	1	6	3
65 „ (29·5 „) ..	—	—	—	—	—	—	2	—	—
70 „ (31·8 „) ..	—	—	—	—	1	—	1	1	1
75 „ (34·1 „) ..	—	—	—	—	—	—	—	1	—

The 29 children of 50–55 lb. (22.7–24.9 kg.) would have received, with a dosage based on age, six different doses. The eldest would have received (at 0.05 g. per year, minus 0.05 g.) more than 150% more than the similarly weighted youngest. The 35 children of 5 years would all have received the same dose (200 mg.). This "same" dose would have varied from 6 mg./kg. to 14 mg./kg. An experienced anaesthetist may vary his rough guide "according to the general type and size" with safety and accuracy, but how much easier to base the guide itself on weight in the first instance.

While there is an indisputable tendency for children to grow up, and for older children to weigh more than younger ones, the great scatter of weights shown above (particularly in the group from which most tonsillectomies are derived) is too great, in my opinion, to serve as a basis for the discriminate administration of potent drugs.—I am, etc.,

Portsmouth. R. J. HAMER HODGES.

SIR,—My hope of avoiding a space-consuming correspondence on tonsillectomy technique was not great, and has turned out to be forlorn. I do not know when this correspondence will be ended by editorial ukase, but before that happens may I extend a welcome to anyone interested, including Mr. H. V. Forster (*Journal*, July 23, p. 265), who kindly expressed the desire, to visit me on a Wednesday at 11 a.m. for a demonstration of the Waugh technique of dissection and for discussion? I should be grateful if intending visitors would write to me at the Hospital for Sick Children, Great Ormond Street, London, W.C.1, to fix a date.—I am, etc.,

London, W.1. JAMES CROOKS.

Snake-bite

SIR,—In a letter (*Journal*, July 16, p. 204) Dr. Abdul Wahab Ariff reported 32 cases of death from snake-bite, "mostly from the bite of the Mayalan pit vipers," in Perlis, Malaya, between 1946 and 1954.

I do not believe that any authenticated case of death in man from the bite of either the Malayan pit viper, *Ancistrodon rhodostoma*, or the other Crotalidae found in Malaya, has been reported previously. M. W. F. Tweedie, of the Raffles Museum, Singapore, says that he has never heard of death following its bite,[1] and that "the bite is not dangerous to human life."[2] M. A. Smith,[3] writing of the bite of the pit vipers of South-east Asia generally, states: "Deaths have been recorded; but they are extremely rare, and they appear to have been caused by septic conditions secondary to the bite. In the vast majority of cases the symptoms are not severe, and are quickly recovered from."—I am, etc.,

Cambridge. E. R. S. HOOPER.

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2 —— and Harrison, J. L., *Malayan Animal Life*, 1954, p. 97. Longmans, London.
3 Smith, M. A., *Reptilia and Amphibia*, 1943, vol. 3, p. 479.

Diabetes and Pregnancy

SIR,—In a recent issue summaries of communications at the Toronto Meeting were reported. Mr. J. H. Peel (*Journal*, July 2, p. 44), discussing "The Management of the Diabetic Patient in Pregnancy" in the Section of Obstetrics and Gynaecology, is reported as saying that "modern methods have reduced the maternal mortality to less than 1%." He then referred to the indications for "therapeutic" abortion. Peel states that the following factors have to be considered before deciding that therapeutic abortion is indicated in any case: (*a*) the family history of diabetes; (*b*) the presence of vascular complications; (*c*) the co-operativeness of the patient; (*d*) the previous obstetric history; (*e*) the size of the family. Does this mean that he considers it clinically justifiable to procure an abortion because the mother may bear a potential diabetic; because there has been a bad obstetrical history with many foetal losses; because the mother has already borne "enough" children; or because the mother is uncooperative?

Apropos of patients with bad obstetrical histories, a woman delivered of a live child at the National Maternity Hospital, Dublin, in 1954 had a history of four unsuccessful pregnancies outside our service. Would Peel have advised abortion in such a case? It is conceded that patients with established vascular complications are difficult problems. Nevertheless they can be carried safely through pregnancy with careful and rigorous control of the diabetes. Priscilla White[1] holds that there is only one contraindication to pregnancy in a diabetic—that is, nitrogen retention or other evidence of renal failure. In such a case the "end" is already in sight and pregnancy does not influence matters significantly. The writer believes that there is no medical case for therapeutic abortion in diabetics.—I am, etc.,

Dublin. M. I. DRURY.

REFERENCE

1 White, P., *Diabetes*, 1954, 3, 453.

Acute Hepatic Failure

SIR,—While appreciating the otherwise excellent article on "Acute Hepatic Failure" by Dr. Sheila Sherlock (*Journal*, June 4, p. 1383), and in particular the stress laid on the cerebral changes and fetor hepaticus, I was concerned that there was no mention of spontaneous acute abdominal pain, which, not uncommonly, is the first definite sign of acute liver failure. There may be no previous indication during the course of the underlying liver disease of this severe complication, and indeed the liver disease may not have been recognized. Therefore it should be made more generally known that acute necrosis of the liver with liver failure may produce such acute

upper abdominal pain that a mistaken diagnosis of perforated abdominal viscus or other acute emergency is made: if surgery is then undertaken the diagnosis at once becomes obvious when the abdomen is opened, but the chance of recovery is greatly reduced. I have only recently seen such a mishap occur, and this even after the admitting staff of the hospital had been informed of the probable and subsequently correct diagnosis.

In my experience, the presence of fetor hepaticus can often be detected before the onset of more obvious signs, but only if it is deliberately sought: it is a quite unmistakable odour and should be a "must" for every final-year student.—I am, etc.,

Toronto, Canada. GEOFFREY FFRENCH.

Sensitivity to Combined Antibiotics

SIR,—I refer to the report by Dr. Leonard Haas (*Journal*, July 23, p. 245) on a case of osteomyelitis of the maxilla with cavernous sinus thrombosis in infancy, and to his use of antibiotics. According to this report, combined treatment with streptomycin and chlortetracycline was instituted after *in vitro* tests of the sensitivity of the organisms concerned to various individual antibiotics, but not to these two in combination. A favourable response was followed by a relapse while the infant was still on the same treatment. Recourse was had to chloramphenicol alone and the condition cleared. Two subsequent relapses responded to chlortetracycline alone, but in both instances occurred after treatment had been stopped.

Dr. Haas writes: "The case described illustrates the importance of basing the antibiotic treatment on bacteriological sensitivity tests . . ." I agree with him, but I think that he should have been more explicit, and should have pointed out that his treatment was not so based; the failure of the combination of streptomycin with chlortetracycline illustrates very well a danger. I mean the danger of combining a bactericidal with a bacteriostatic antibiotic on the strength of *in vitro* evidence of their separate activity. This danger is not sufficiently well known, and we should not miss an opportunity of reminding ourselves of it.—I am, etc.,

Sittingbourne, Kent. DEREK CLARKE.

Penicillin Anaphylactoid Shock

SIR,—I read with interest and some apprehension the reference to penicillin anaphylactoid shock in the article by Drs. Rowland J. Calvert and Eric Smith (*Journal*, July 30, p. 302). While I agree it is incumbent to take all possible precautions in the administration of penicillin, I should like to point out that it is impossible for the busy G.P. or district nurse to spend 20 minutes in a patient's home after administering an injection.—I am, etc.,

Richmond, Surrey. R. G. ORR.

SIR,—The most interesting and careful review of anaphylactoid reactions and penicillin by Drs. Rowland J. Calvert and Eric Smith (*Journal*, July 30, p. 302) will, I hope, bring to the Editor's table every bit of additional knowledge. One case within my knowledge began his anaphylactoid reaction only when, well on in a course of penicillin, the penicillin was from another manufacturer. The doctor in attendance was convinced that the change in the source of supply was the determining factor. Has this fact any possible significance?

My next point is the association of epidermophytosis and anaphylactoid reactions to which they refer. The authors state in reference to their case "exhaustive inquiry revealed . . . There had been no known epidermophytosis." They do not state whether they themselves had actually examined his feet carefully. It is most unlikely that "a robust Army officer aged 47" has not had, or has not got, epidermophytosis to some extent. Again there is no statement in their article as to whether any inquiry, when investigating the coincidence of epidermophytosis, had recognized the existence of the subungular species or that the interdigital fungus has itself a number of different species, with varying effects on the host. An investigation some years ago in the R.A.F. (personal communication) of a large new entry of lads showed nearly 90% with some degree of infection with this fungus and that the great majority were unaware of being so infected. My own experience is that the majority of patients are unaware of their infection, particularly if it is of the subungual type.

Now we know the power and potentialities for good and ill of the "fungus" world, this knowledge should provide a real stimulus to review our appreciation of the many species and types of fungus that affect the human body, from ringworm to onychogryphosis.—I am, etc.,

Chipping Camden, Glos. C. B. HEALD.

Labelling the Container

SIR,—So impressed am I by the reasons put forward thus far regarding the use of "*nomen proprium*" (*Journal*, July 16, p. 204) that I am impelled to make comment. Apart from being a considerable "time-saver" and "memory-jogger" (in the case of "repeats," where records for a multiplicity of reasons are not available), there is to my mind an infinitely greater consideration—the case of overdosage. In such a case the finding of a container with label showing the contents might well mean valuable time saved in determining the offending drug.

Indeed "N.P." should become a golden rule. Some time ago the local medical committee in this area requested the pharmacists to label thus. A considerable number are still doing so, and their co-operation is greatly appreciated. I have recently asked a pharmacist friend whether he would ignore such a request on a prescription. In unmistakable words (unprintable) and tone he assured me that not only would he carry out the request but that in his opinion the pharmacist who failed to do so would not be carrying out the full directions, and in the case of a fatality such failure might well occasion knuckle-rapping and unenviable publicity. But let it not be a direction; let it be a courteous request: "N.P., *please*." I cannot agree with Dr. M. E. Lampard (*Journal*, July 23, p. 265) that considerable pressure will have to be brought on the chemists to bring this about.—I am, etc.,

West Bromwich. H. S. M. MAXWELL.

SIR,—I read with interest Dr. Alistair G. Cruikshank's letter (*Journal*, July 16, p. 204). I started to use the abbreviation N.P. after reading his paper in the *Practitioner*. After a week or so I discovered to my dismay that the local pharmacists (I spoke to six) were unfamiliar with the term, nor did it appear in the *Pharmaceutical Pocket Book*. Clearly from Dr. Cruikshank's letter it is understood in Edinburgh, but he is not correct in supposing that every pharmacist knows it—not in England anyway.

I agree that it is often helpful to label a drug with its proper name, but at present there is no generally accepted term. Could the appropriate medical and pharmaceutical bodies take this matter up and agree on an abbreviation which the profession could use with confidence?—I am, etc.,

Derby. G. N. L. GODBER.

"Over-the-counter" Spectacles

SIR,—I think that Dr. W. S. Inman's letter (*Journal*, July 23, p. 267) is too sweeping in generalization. Grown-ups may not have eyes visually damaged by wrong glasses, and may only suffer pain or discomfort, but with children it is quite otherwise. Every child's eye is a growing eye; it is often a stretching and a "sick" eye; and small errors of astigmatism may start trouble which becomes more serious in school-life, or later.

For many years there has been a dictum: "Low hypermetropia proceeds to low myopia through the turnstile of low astigmatism." It is therefore of the gravest importance that low errors of astigmatism should be corrected in children, and, I consider, in young adults if producing symptoms.—I am, etc.,

Southampton. JOSHUA KEYMS.

Physique of Children

SIR,—May I reply on behalf of my colleagues, two of whom are on holiday on the Continent, to your correspondents? Dr. E. S. Lower (*Journal*, July 16, p. 204) rightly suspected a mistake in the text of our article (*Journal*, June 25, p. 1506). The table is correct, and the misleading sentences should read: "It is interesting that many Ml girls did well in the intelligence and English tests, but few did so in arithmetic and the practical ability test. The slightly less muscular and more linear girls of sector Lm, on the other hand, performed if anything rather better in arithmetic and in practical ability than in English and the intelligence test." Dr. Lower also asks whether the total number of place winners contained a minority or a majority who were considered good at games. The answer is a minority, 22% of boys and 34% of the girls, but as previously indicated no exact conclusion may be drawn from these figures because the criterion of athletic ability varied widely from school to school.

Dr. J. N. Mills (*Journal*, July 23, p. 265) raises an important point concerning statistical method and prefers the χ^2 test. Having applied it to intelligence scores he confirms our findings among girls by reporting a highly significant unevenness of distribution among their somatotypes; but the χ^2 test fails to establish any such unevenness among a smaller sample of boys. If our interest in the Lf boys and girls had been stimulated solely by the data in the present paper, Dr. Mills would have been right in pointing out that it is quite probable that, in random data, some group would show a performance well above average. However, as mentioned at the outset, we were prompted to carry out the investigation by independent evidence from a survey of undergraduate performance; in this survey undergraduates of physique most similar as far as can be judged to Lf children had done much the best. We had, therefore, a working hypothesis in advance that a certain type of boy, and possibly girl, too, might do particularly well (which they did), and in this situation the significance test we applied seems fair.

We recognize that the most our results so far can do is to stimulate interest and, without making any great claims, record our impression that performance in various kinds of scholastic and intelligence tests might profitably be studied in larger samples according to finer shades of physical classification, distinguishing first, for example, between central and peripheral somatotypes. The small but significant trends we have found derive their importance from their influence in the large number of borderline cases who just succeed or fail to obtain grammar or technical school places. A system of scholastic selection which at the age of 11 appears to regulate children's lives in a formidable way, without regard to early or late development, a system which shows a tendency to select children of particular character often with less than average "muscularity," demands careful scrutiny, and the whole difficult problem is brought to a head by the fact that education grants are only available to roughly one-fifth of the children about whose promise of growth, general development, and actual chances of fulfilment we know only too little.—I am, etc.,

Oxford. R. W. PARNELL.

Comforters

SIR,—I was particularly interested in Dr. Nigel Swallow's recognition (*Journal*, July 23, p. 266) that the objects that small children drag around with them everywhere are of significance. In this, as in so many other respects, infants and children can teach us, if we observe without being hampered by a need to teach or correct.

In child psychiatry this phenomenon, to which Dr. Swallow refers, is known to be very important as part of the normal child's developing capacity to relate to a world that is external. The objects can be said to be half-way between me and not-me. They stand at one and the same time for the real mother, or a part of her, and for the internalized version of her which in favourable circumstances is all the time building up and forming the basis for belief, and for the capacity to suffer loss without loss of part of the self.

I have personally referred to these matters in an article entitled "Transitional Objects and Transitional Phenomena"[1] and examples are given in a further article by Olive Stevenson.[2] Reprints of these articles are available should interested readers of the *British Medical Journal* find the journals referred to difficult of access.—I am, etc.,

London, S.W.1. D. W. WINNICOTT.

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[1] Winnicott, D. W., *Int. J. Psycho-Anal.*, 1953, **34**, 89.
[2] Stevenson, O., in *Psychoanalytical Study of the Child*, 1954, **9**, 199.

Prophylactic Packets

SIR,—The submission by the Association of Moral and Social Hygiene that men in the Services should not be protected from venereal diseases (*Journal*, July 30, p. 334) savours of intolerance. It is hoped that the Services will attach no importance to it. Although, no doubt, many men remain continent for moral reasons, it is most undesirable to use the fear of disease as a weapon to impose chastity. It is suggested that to withhold prophylactic penicillin would be as unethical as withholding prophylactic quinine in a malarial area.—I am, etc.,

Fareham. G. G. THYNE.

Activity of Piperazine

SIR,—The results of experiments using three salts of piperazine, the citrate, adipate, and phosphate, *in vitro* against *Ascaris lumbricoides* (O. D. Standen, *Journal*, July 2, p. 20) showed clearly that these three salts of different solubility were indistinguishable in their activity under the well-defined experimental conditions employed. The report was concerned primarily with the effect of piperazine on the parasite, and with speculation as to how far such observations were of use in choosing the optimal time for dosage in relation to speed of bowel movement and absorption of drug.

In his letter (*Journal*, July 16, p. 205), Dr. Frank Hartley offered criticisms of these findings by attributing to the adipate characteristics of solubility *in vivo* that do not apply to other salts. Dr. Hartley presents no experimental evidence for his categorical statement: "The sparingly soluble adipate, by contrast, becomes coated with the more insoluble adipic acid in contact with the gastric contents and is therefore much less absorbed."

The solubility of piperazine adipate in *water* at 37° C. has been stated to be 7.49 g./100 g. solvent.[1] This we have confirmed, and found the solubility of piperazine adipate in 0.2% w/v HCl at 37° C. to be very similar—that is, 7.76, 7.65, 7.49 g/100 g. solvent in three separate experiments. Adipic acid in 0.2% HCl at 37° C. gave solubilities of 3.25, 3.24 g./100 g. solvent. Piperazine adipate contains 62.9% of adipic acid; therefore 7.5 g. of salt contains 4.7 g. of adipic acid, of which 3.25 g. will dissolve in 100 ml. of 0.2% HCl irrespective of the presence of piperazine.

In experiments in the laboratory, the following results were obtained: (1) 7 g. of piperazine adipate were gently shaken with 100 ml. of 0.2% HCl at 37° C. All the salt except a few large crystals dissolved in 30 seconds. Solution was complete in 2½ minutes. (2) 0.7 g. of piperazine adipate, gently shaken with 10 ml. of human gastric juice (free acid 0.02%; total acid 0.1%), dissolved rapidly, but was not completely soluble at 37° C. In similar conditions, 0.6 g. dissolved completely in 30 seconds. (3) Two "entacyl" tablets (each equivalent to 0.3 g. piperazine adipate, total weight 0.79 g.) gently shaken with 10 ml. of 0.2% HCl at 37° C. began to disintegrate and dissolve immediately. After half an hour the solution was filtered from the small amount of insoluble residue, evaporated and dried. The weight of the dried filtrate was 0.63 g., equivalent to 105% of the label strength of piperazine adipate. The weight of the insoluble residue was 0.183 g. (4) Two entacyl tablets (total weight 0.81 g.) in 10 ml. of human gastric juice shaken intermittently appeared to be completely disintegrated in half an hour. The liquid was filtered through a Gooch crucible with the aid of 2 ml. of 0.2% HCl and the insoluble residue after drying weighed

0.104 g. (5) A quantity of entacyl suspension equivalent to 1 g. of piperazine adipate when mixed with 13.4 ml. of 0.2% HCl and warmed to 37° C. produced a clear solution.

We cannot see any evidence for the contention that the adipate becomes coated with adipic acid, or that it is rendered insoluble in the gastric contents.

In order to compare the rates of absorption of piperazine preparations, the citrate, adipate (entacyl), phosphate, and the citrate elixir (antepar) were given to groups of 10 normal adult volunteers, each of whom received a dose equivalent to 3 g. of piperazine hydrate. The urine was collected at intervals for 24 hours, and the excretion products of piperazine determined in each sample colorimetrically with sodium 1:2-naphthoquinone-4-sulphonate. Naturally occurring chromogens were accounted for by using internal piperazine standards in each determination in a manner similar to that described by Harris and Raymond[2] for the determination of nicotinic acid with cyanogen bromide and *p*-aminoacetophenone. With all the preparations, excretion began in most subjects within half an hour; the rate was maximal between 1 and 8 hours, and excretion was virtually complete in 24 hours. The mean percentages of the dose excreted and their standard errors were as follows: citrate: 42.8 ± 5.53; adipate: 33.1 ± 7.35; phosphate: 30.5 ± 4.27; citrate elixir: 21.6 ± 4.22. There was no significant difference between the rates of excretion of citrate, adipate, and phosphate, and, as colour-producing substances appeared in the urine, it is evident that equivalent amounts of piperazine from all of these salts had been absorbed into the blood stream.

When Dr. Hartley says: "Both citrate and phosphate, being soluble in the gastric contents, suffer much absorption before reaching the intestinal parasites," it is of interest to inquire where he supposes the absorption to take place. We can only assume that he means in the stomach, which is not a good absorptive organ for drugs. We put this matter to the test by administering 3 g. of piperazine hydrate, neutralized with hydrochloric acid, to four volunteers immediately after a meal of fish and chips to delay the emptying-time of the stomach and thus give the maximum opportunity for absorption of piperazine by the gastric mucosa. Urine collected at half-hourly intervals showed that no excretion-products appeared for 1–1½ hours. It seems very unlikely, therefore, that any significant amounts of the drug are absorbed in the stomach.

We consider that the results of these experiments show Dr. Hartley's claims to peculiarities of solubility and absorption of piperazine adipate to be unfounded. He makes much of the neurotoxic action of piperazine citrate; in fact side-effects are uncommon and trivial, and have only occurred when excessive and prolonged dosage has been given. It is unlikely that such large doses of the adipate have been administered in clinical practice. The pharmacology of piperazine is of great interest, and if it is true that the adipate is a more versatile anthelmintic than the citrate an explanation based upon careful experiment will be needed. Speculations of the kind made by Dr. Hartley, in the absence of supporting data, merely serve to confuse the issue.—We are, etc.,

O. D. STANDEN. E. W. ROGERS.
L. G. GOODWIN. D. STEPHENSON.

London, N.W.1.

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1 Davies, M. T., *et al.*, *J. Pharm. Pharmacol.* 1954, **6**, 707.
2 Harris, L. J., and Raymond, W. D., *Biochem. J.*, 1939, **33**, 2037.

Opportunities for Medical Practice

SIR,—By direction of the Executive of the Council of the Victorian Branch of the British Medical Association I am writing to support the views of Dr. J. H. S. Geggie, of Canada, in his letter (*Journal*, July 9, p. 142) in reference to the article by Sir Stanley Davidson, "Opportunities for Medical Practice at Home and Abroad" (*Journal*, May 14, p. 1171).

Sir Stanley's views on medical practice in Australia were based largely on an article by Sir Hugh Poate published in 1953, but the forecast of a surplus of doctors made in that article has not been borne out. The position in Victoria can be said to be closely comparable to the position in Canada as stated by Dr. Geggie, and it is hoped that those British graduates who may be contemplating emigrating will not be discouraged by Sir Stanley Davidson's views. Examination of the advertisement columns of the *Medical Journal of Australia* will give some indication of the opportunities available.—I am, etc.,

C. H. DICKSON,
Medical Secretary,
Victorian Branch.

Melbourne, Australia.

REFERENCE

1 Poate, H., *Med. J. Aust.*, 1953, **1**, 714.

Environmental Cancer Research

SIR,—Sir Ernest Kennaway (*Journal*, July 2, p. 56) has pointed out that cancer of the cervix is rare among Jewish women. Cancer of the penis is infrequent among circumcised males, Jew or Gentile.[1] Generally the incidence of cancer of the penis is lower than that of the cervix.

Animal experiments have shown that undifferentiated epithelium is highly susceptible to chemical carcinogenesis.[2] According to Plaut *et al.*,[3] smegma has carcinogenic properties. Cancer of the cervix may therefore be caused by the action of smegma on undifferentiated epithelium. If intercourse takes place during or immediately after menstruation we have an instance of carcinogen applied to basal cells. With orthodox Jewish women there is no exposure, because Talmudic law prohibits contact before the 12th day of the cycle. As to the male genital tract, injury or maceration of the prepuce may expose the basal undifferentiated substrate to the action of carcinogenic smegma. In the circumcised this would not occur. The higher incidence of carcinoma of the cervix as compared to that of the penis may be due to the monthly denudation of the cervical epithelium,[4] which is a regular physiological process, whilst loss of surface epithelium from glans or prepuce is an occasional pathological feature. These considerations might remove some of the criticisms raised against Professor Kennaway's "mouse painting theory." It seems therefore desirable to make a fuller investigation into the frequency of contacts in the immediate post-partum and post-menstrual period among women who suffer from cancer of the cervix.—I am, etc.,

R. STEIN-WERBLOWSKY.

London, N.W.3.

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2 Breedis, C., *Proc. Amer. Ass. Cancer Res.*, 1955, **2**, 7.
3 Plaut, A., and Kohn-Speyer, A. C., *Science*, 1947, **105**, 391.
4 Wollner, A., *Amer. J. Surg.*, 1942, **57**, 331.
5 Kennaway, E., *British Medical Journal*, 1955, **1**, 1107.

Visit of Russian Doctors

SIR,—Most doctors will share the sentiments expressed by you in the leading article (*Journal*, August 6, p. 369) on the forthcoming visit of the Russian doctors, and will join you in welcoming the guests. You did not mention, however, that many eminent Russian doctors have visited this country in recent years and that these visits have already contributed significantly to better mutual understanding and helped to prepare for the desired wider exchange of visits and knowledge. Your editorial does not do justice to all the doctors in the medical schools, hospitals, and private surgeries who were hosts and displayed traditional medical hospitality to their Russian guests when to do this was less popular than now. As an example, one might mention the visit of 12 Russian doctors who came here last December as guests of the Society of Cultural Relations with the U.S.S.R. The leader of this delegation, Professor A. Shabanov, reported on their experiences in two articles published by the *Meditsinsky Rabotnik* on June 14 and 17. He concluded in the following terms.

"We spent 20 days in England, crossed the country twice by train, visited eight towns, and saw the work of many hospitals and scientific institutions. We met and spoke with many people: scientific workers, professors, family doctors, teachers, students, Manchester and Scottish miners, taxi-drivers, councillors of local authorities, and housewives. And the deepest feeling we brought away is one of great respect for the English people, for their great history and future.

"We have brought away with us the conviction that the simple and honest English people sincerely want peace and

mutual understanding between different countries, and strive for further development of friendly relations with the multinational Soviet Union. We are certain that the extension of friendly and scientific relations between the medical workers of Great Britain and the Soviet Union will undoubtedly help in furthering better understanding between our nations and contribute towards the relaxation of international tension."—I am, etc.,

London, S.W.16. L. CROME.

A.I.D.

SIR,—Whatever approval may be given by the American Society for the Study of Fertility, and by others all over the the world who are popularizing artificial insemination (for example, Dr. Philip Bloom, *Journal*, July 23, p. 264), we shall always have to face the fact that a married woman who allows herself to be inseminated by a stranger commits adultery. In some countries the doctor who materially assists in the introduction of the semen can be cited as a co-respondent.

The offer of adoption of a baby without the attendant risks of pregnancy, labour, stillbirths, etc., will ever remain open to those whose marriages are childless. There are, of course, many other objections to A.I.D., most of which appeared before in your correspondence columns when the matter was well ventilated in 1944–5.—I am, etc.,

Slough, Bucks. N. C. HYPHER.

Whipple's Disease

SIR,—We read with interest your annotation on Whipple's disease (*Journal*, July 16, p. 191), as we are at present studying some aspects of this entity rarely recognized in Britain. The importance of the sudanophilic material in the lacteals and mesenteric nodes has possibly been over-emphasized—in one of our small series of cases there was, for example, no demonstrable lipoid material at either of these sites, but the infiltration by glycoprotein-filled macrophages was intense, and the steatorrhoea of exceptional severity. Again, as far as we are aware, no investigations of the reticulin pattern have so far been carried out, but there would appear to be a great increase in the reticulin network and marked disruption of the normal architecture of the mesenteric nodes.

We should be glad of the opportunity to carry our investigations further, and would welcome the chance to study additional case material for this purpose.—We are, etc.,

P. FARNAN.

Southampton. R. A. GOODBODY.

POINTS FROM LETTERS

Ball-bearing in Ear

Dr. ABDUL WAHAB ARIFF (Negri, Malaya) writes: I would like to report the case of a Chinese boy of 5 years old who came to see me with a ball-bearing in one of his ears. Repeated attempts were made to extricate it under general anaesthesia by means of several kinds of aural apparatus, but they all failed. While about to give up hope and hand him over to a specialist, I managed to borrow a pair of magnetic forceps from a radio mechanic. . . . The ball-bearing was immediately attracted to the point of the forceps and drawn out with ease. It would not be a bad idea to design a magnetic aural (or nasal) forceps based upon the above principles with a view to avoiding unnecessary pain and misery to the young victims.

Hypodermic Injection Technique

Dr. W. E. MCCULLOCH (Jamaica) writes: Mr. G. H. Colt's letter (*Journal*, July 2, p. 61) prompts me to write. He might well have taught me the following trick, but I forget where I learnt it. Inject between the hair roots and no pain is felt. Hairs are better seen while the skin is still wet from the cleansing alcohol, but do not inject then—it will be painful. In children who can understand I always freeze the site of injection with ethyl chloride, with the promise that they will see snow, usually for the first time in their lives out here, and inject as the snow melts, not before.

Obituary

Sir REGINALD BOND, K.C.B., M.B., F.R.C.P. F.R.C.S.Ed., D.P.H.

We record with regret the death in a Worthing nursing-home on July 27 of Surgeon Vice-Admiral Sir Reginald Bond, formerly Medical Director-General of the Navy. He was 83 years of age.

Reginald St. George Smallridge Bond was born at Ogbourne St. George, Wiltshire, on April 10, 1872, the son of the Rev. Alfred Bond. Entering Edinburgh University as a medical student in 1889, he was awarded the Mackenzie bursary in anatomy, and graduated M.B., C.M. in 1894. He then held the appointment of house-surgeon at Edinburgh Royal Infirmary, and, having obtained the certificate in psychological medicine of the Medico-Psychological Association, became assistant physician at the Royal Morningside Mental Hospital and, later, assistant medical officer at Caterham Mental Hospital. Up to that time the pattern of his career had followed closely that of his elder brother, the late Sir Hubert Bond, who became a senior commissioner of the Board of Control, but in 1898, having obtained the F.R.C.S.Ed. in the previous year, Reginald Bond entered the Royal Navy as a surgeon.

[*Walter Stoneman*

By 1914, when the first world war broke out, Bond had attained the rank of surgeon commander, and from then until 1916 he served in H.M.S. *Commonwealth*. From 1916, the year in which he took the D.P.H. of the English Royal Colleges, until the end of the war he was senior medical officer at the Royal Naval Hospital, Plymouth. He was elected a Member of the Royal College of Physicians of London in 1919, the year in which he was naval health officer on the commander-in-chief's staff at Plymouth. He was admitted to the Fellowship in 1927. Bond's two main interests were hygiene and the law. From 1921 to 1923 he was director of medical studies and professor of hygiene at the Royal Naval Medical School, Greenwich. He was called to the Bar by Gray's Inn in 1922, and in the same year was awarded the Gilbert Blane Medal by the Royal College of Surgeons of England for his valuable services in designing and perfecting an air-pumping apparatus for submarines. He also received the thanks of the Lords of the Admiralty for his work. It is a matter of some interest that of the four Blane Medals awarded in 1922—the first to be awarded since 1914—three should go to officers who were to become Medical Directors of the Navy—namely, Bond, the late Sir Robert Hall, who died in 1951, and Sir Sheldon Francis Dudley. After holding office as deputy from 1923 to 1926, Bond became Medical Director-General of the Navy in 1931 in succession to the late Sir Arthur Gaskell, who died in 1952. Between these two appointments he was in charge of the Royal Naval Hospital, Plymouth, with the rank of surgeon rear-admiral. He was an Honorary Physician to the King from 1931 to

1934, when he was placed on the retired list with the rank of surgeon vice-admiral, and Sir Robert Hall then succeeded him as Director-General.

In 1932 Bond was appointed to the general council of Queen Mary's Hospital, Roehampton, as the representative of the Admiralty; four years later he became a governor of the hospital; and from 1942 to 1948 was its honorary secretary and treasurer. He resigned from both the general council and the board of governors in 1953. He was treasurer of Epsom College from July, 1941, to February, 1946, when he relinquished the office on account of ill-health. He had also been chairman of the committee of the Royal Naval Benevolent Society. He was a member of a number of scientific societies, including the Royal Sanitary Institute, now renamed the Royal Society for the Promotion of Health. He was co-editor of the *Journal of the Royal Naval Medical Service* from 1920 to 1926. When the British Medical Association held its Annual Meeting at Portsmouth in 1923 he served as a vice-president of the Section of Naval and Military Hygiene. He was appointed C.B. in 1926 and promoted K.C.B. seven years later. In 1900 he married Miss Blanche Alexandra, the only child of Captain John D'Arcy-Irvine, R.N. There were no children of the marriage, and Lady Bond died only a week before her husband.

J. D. MARTIN-JONES, M.D., D.O.M.S.

We record with regret the death at his home at Salisbury, Wiltshire, on July 24 of Mr. J. D. Martin-Jones, ophthalmic surgeon to the Salisbury group of hospitals. He was 48 years of age.

John Dennis Martin-Jones was born on March 29, 1907, the elder son of the late Dr. Martin Llewelyn Jones, who died in March last year, and was educated at Emmanuel College, Cambridge, receiving his clinical training at St. Bartholomew's Hospital. He took an honours degree (Natural Sciences Tripos) at Cambridge in 1930 and qualified M.R.C.S., L.R.C.P. in 1934. Two years later he obtained the degrees of M.B., B.Chir., in 1938 he took the D.O.M.S., and in the following year he proceeded to the M.D. After holding the post of senior house-physician at St. Bartholomew's under Dr. C. M. Hinds Howell, he went to the Royal Westminster Ophthalmic Hospital as house-surgeon, later becoming senior house-surgeon, resident medical officer, and registrar. During this period he held the Cruise Research Scholarship, and he was also refractionist to St. Bartholomew's and St. Mary's Hospitals. During the second world war he served in the R.A.M.C., with the rank of major, from February, 1940, to October, 1945, mostly in the Middle East. For six months he was in charge of a mobile ophthalmic unit during the invasion of Normandy, dating from a few days after "D" day. He next became command specialist in ophthalmology, Western Command, and surgeon in charge of the ophthalmic centre at Chester. He was appointed surgeon in charge of the ophthalmic department at Salisbury General Infirmary in April, 1946, on the retirement of Mr. G. Conroy Dixon. He was in addition oculist to the Wiltshire County Council and ophthalmic surgeon to the Ministry of Pensions and to Odstock Hospital.

We are indebted to Mr. R. Foster Moore for the following appreciation: It is melancholy to report the death of one in the prime of life who had attained the top rank in his branch of the profession, whose home life was his chief joy, and who was held in most affectionate regard by all who knew him. On July 24 John Dennis Martin-Jones, feeling a little indisposed, was persuaded by his wife to have his breakfast in bed; when next she went up he had passed away. He had worked very hard and for the last few years had felt the stress of life, but had not allowed it to curtail his work, nor had his friends felt any grave anxiety with regard to him. His annual holiday was imminent, and it was thought that this was what was needed to restore him.

One of the great pleasures in life for him was to be able to help someone in some way, and a visit from him was a real and special delight. He seemed to radiate happiness, and one was always glad to find him at the door; he was, indeed, for many a very present help. He had a delightful home life and was very proud of his two small daughters. As to his professional attainments, his knowledge was extensive and was widened by his neurological training. He was thorough and wise, and he had that most valuable of all attainments, a soundness of judgment; his temper was fired by anything which savoured of humbug or self-importance. His monograph on "Uveal Sarcoma," published as a *Supplement* to the *British Journal of Ophthalmology* in 1946, is one of the most notable contributions to this important subject. He was gifted with most delicate hands and was an exquisite operator.

It once fell to my lot to meet him over the examination table, and to put him at his ease, though this was quite unnecessary, I asked him if he could tell me which of the anthropoid apes had the longest tail, to which, with his whimsical smile, he replied: "Well, Sir, I don't know, but you ought to." He had worked hard, too hard, but this could not prevent him from making frequent journeys to Wales to see his father whom he greatly revered and who died a few months ago. To his widow and two small daughters, his mother, and brother, our profound sympathies extend. A host of friends and patients grieve at his parting.

MORITZ BLUMBERG, M.D.

Dr. Moritz Blumberg, one of the last surviving surgeons trained in the famous school of Johann von Mikulicz, died in London on June 14 at the age of 82.

Jacob Moritz Blumberg was born at Posen on June 27, 1873, and graduated in medicine at Breslau University in 1897. He then spent some time in research on the sterilization of surgeons' hands before operations, and published a number of papers on the subject between 1898 and 1902. At that time rubber gloves were little used by surgeons, partly because they tore too easily, but particularly because their slippery surface made efficient work difficult. In 1900 he demonstrated a new type of glove made to his own specification, a glove with a rough surface like those in general use to-day, and for some years it was known as the Blumberg glove. He settled in practice in Berlin as a surgeon and gynaecologist and was much in demand as a consultant. His name is associated with the rebound sign, an early sign of the onset of peritoneal inflammation, and in 1907 he first described the much used, misused, and abused buttonhole incision. He also devised an instrument to facilitate suture of the perineum, and at an international congress of gynaecologists in 1912 he read a paper about a new operation to produce temporary sterility in women.

Blumberg was called up immediately on the outbreak of the first world war in 1913, and since he was a capable organizer he was made commissioner for infectious diseases. His main task was to combat an epidemic of typhus fever which had broken out in prisoner-of-war camps on the eastern front. Faced with the task of having to "de-louse" 10,000 Russian prisoners within 24 hours and to provide them with clean uniforms, he took rather more than the prescribed time, but the extensive powers granted to him made the

task possible within a few days. This work was believed to have averted a major catastrophe, and was later described as "one of the greatest achievements in medical military history." At the end of hostilities Blumberg was presented with an illuminated address by the English, French, Italian, and Russian prisoners of war who were in Brandenburg camp and under his direct command.

On return to his civilian practice Blumberg gave up most of his general surgery for gynaecology, but continued to work in the *x*-ray and radium institute which he founded. His sympathetic, yet firm personality inspired immediate confidence in those who sought his advice. He spent much of his time during the 'twenties in organizing and superintending prenatal treatment centres in Berlin.

When the Nazi regime drove Blumberg from the country he had served so well in war and in peace, he joined his son, Dr. E. F. Blumberg, in England, and later on was able to resume medical work in London. Though over 70, he did much major surgery during the second world war and acquired a considerable practice. He faced the long-drawn-out suffering of his last illness with firmness and great dignity, and his fine sense of humour supported him until the very end.

Dr. J. P. QUINN, of Reedyford, Nelson, Lancashire, died in Reedyford Hospital on June 9 after a long illness. He was 66 years of age. Joseph Patrick Quinn was born in Dublin on November 23, 1888, the second son of Dr. J. P. Quinn of that city. He was educated at Blackrock College and at Trinity College, Dublin, where he graduated M.B., B.Ch. in 1914, taking the D.P.H. six years later. A notable Rugby player, he was capped fifteen times for Ireland, played for the Barbarians, and was a member of the British Expeditionary Force team which beat "The Rest" in 1919. Twice mentioned in dispatches during his service in the R.A.M.C. in the first world war, he was also awarded the Military Cross. In 1921 he went to Nelson as a general practitioner and remained there until his death. Dr. Quinn had a remarkable record of public service. He was a member of both the Lancashire and Burnley executive councils and of the Lancashire and Burnley local medical committees. He was also a member of the Burnley hospitals advisory committee, and a corps surgeon of the St. John Ambulance Brigade. In 1945 he was appointed a serving brother of the Venerable Order of St. John of Jerusalem. Dr. Quinn had a warm and generous nature, and throughout Lancashire his death will be deeply felt by very many friends who admired and respected him. It was indeed a delight to know him.—H. S.

Dr. JOHN SEXTON died at his home at Stourbridge, Worcestershire, on July 24, fifteen days after his 56th birthday. His long and tedious illness was patiently born, and he died as he had lived, an inspiration and an example to all. John Sexton was born on July 9, 1899, and was educated at University College, Dublin, graduating M.B., B.Ch. from the National University of Ireland in 1925. He had been in partnership in Stourbridge for nine years, and previously had practised at King's Lynn, Norfolk, for over twenty years. He was chairman of the West Norfolk Division of the British Medical Association in 1939–40. During his short stay in the Midlands he earned a reputation which few can hope to attain. A man without guile, he was respected and admired by his colleagues, and greatly loved by his patients. Well versed in all branches of medicine, he had a special flair for midwifery. It was an education and a delight to watch him at a case, and no confinement, however awkward, presented any terrors for him. In every way he was the complete general practitioner. He is survived by his widow and three children.—J. K.

Medico-Legal

HOSPITAL EMERGENCY

Hearing at an inquest on August 2 that a house-surgeon who had qualified only three weeks before was in charge of a hospital when a man was taken there after an accident, the Dudley coroner, Mr. A. E. V. Sherwood, indicated there ought always to be someone of experience at a hospital to give emergency treatment. He recorded a verdict of accidental death on William Benjamin Daniel Cooper, a maintenance fitter from Staffordshire, who fell 30 ft. (9 m.) from an overhead crane on July 24.

Dr. Frederick Sowa Boi-Doku, house-surgeon at Corbett Hospital, Stourbridge, said when Cooper was brought into the casualty department his condition was serious. As the resident surgical officer was away for the week-end and the consultants were in Birmingham, he got in touch with the resident surgical officer at the Guest Hospital, Dudley. Dr. Boi Doku thought Cooper's condition good enough to stand the strain of the journey, and he was transferred 10 minutes after admission. When admitted to the Guest Hospital Cooper was seriously shocked and almost pulseless, and died five minutes later.

Asking that his comments should be conveyed to the hospital management committee, the coroner said it was wrong that a young inexperienced surgeon should be placed in such a position. "Whether this is a fault of the management committee or other authorities it ought to be remedied. I don't blame the doctor so much as the system which puts him in this position where he has to make such important decisions. I hope we can revert to the system which operated before the National Health scheme when there was always someone at a hospital to give treatment in cases of emergency."

Universities and Colleges

UNIVERSITY OF OXFORD

In Congregation on July 16 the following degrees were conferred:

B.M.—T. W. Anderson, R. Scott, H. M. Holden, D. Fairbairn, J. E. S. Varley, J. Viner, C. P. McEvedy, J. I. H. Hadfield, B. P. Luxton, M. Kinsbourne, W. G. Rhys-Jones, J. T. Buffin, W. J. C. Thomas, W. S. R. Craig, Margaret A. Mitchell, Molly Painter, Flora M. Sykes, Mary Keene, *H. B. Griffith, *M. J. Yates, *J. D. Macaulay, *W. S. Sykes, *D. G. Penington, *J. A. Hopson.

The Radcliffe Scholarship in Pharmacology has been awarded to Walford John Harrison (Balliol College).

*In absence.

UNIVERSITY OF CAMBRIDGE

Dr. D. H. Clark has been appointed an Associate Lecturer in Psychiatry and Mr. J. F. R. Withycombe an Associate Lecturer in Surgery in the Department of Medicine with tenure from October 1, 1955, for as long as they remain consultants to the United Cambridge Hospitals.

UNIVERSITY OF GLASGOW

On July 9 the Diploma in Public Health was awarded to K. F. X. Bourke, D. P. Brunton, W. R. Falconer, D. J. B. Fletcher, A. N. Hunter, I. S. Macdonald, Sheila F. Schofield, D. J. L. Tredoux, C. Weymes, S. M. Young.

UNIVERSITY OF ABERDEEN

Graduation ceremonials were held on July 7 and 8, when the following degrees were conferred:

M.D.—[1]I. R. Innes, [1]A. A. Shivas, [2]K. C. Watson, W. H. P. Minto.

M.B., CH.B.—[1]R. G. Lascelles, [1]Violet McA. Wyllie, [2]K. D. Sargison, [2]Valerie M. M. Kay, [2]Janet Wynne-Edwards, [2]J. A. Wood, [2]R. C. Campbell, [2]G. Cowie, Nancy Badenoch, Margaret E. Beveridge, R. G. Bruce, A. W. Clubb, Isla Craig, C. S. Crockett, Patricia M. Cumming, Margaret I. Davidson, R. M. Davidson, T. L. Fallowfield, J. A. Findlay, G. L. Forrai, A. Geddes, Doris M. Geddes (formerly Moorhouse), H. R. Gibson, J. M. D. Gill, D. G. Gray, R. Gray, D. Hall, I. E. Holiday, W. A.

Irvine, Elizabeth D. Jamie, Sheila Jones (formerly Clouston), Margaret E. Keay, L. G. Laing, A. N. Laird, G. J. B. Leslie, A. I. Littlejohn, F. P. Lynch, Elizabeth M. McConachie, J. B. MacDonald, D. McLeman, W. D. Masson, Elizabeth W. Michie (formerly Robertson), A. M. Milne, D. D. Milne, Ivy R. Moody, H. D. R. Munro, C. Murray, Mary A. B. Murray, W. D. Ogston, T. W. Patey, Dorothy M. Porter, Anna I. Robertson, C. F. Roe, D. I. Ross, I. Ross, G. B. Scott, A. Sinclair, W. Strachan, I. Stuart, S. S. Sutherland, J. M. Taylor, C. D. Thomson, J. McN. Thomson, Moira M. Wilson.

[1]With honours. [2]With commendation.

UNIVERSITY OF DUBLIN

SCHOOL OF PHYSIC, TRINITY COLLEGE

The following medical degrees were conferred on July 5:

M.D.—H. G. Nelson, A. T. F. ffrench-O'Carroll, R. J. Weir.

M.CH.—J. W. Jackson.

M.B., B.CH., B.A.O.—B. E. Barrett, Aileen E. F. Benson, Anne H. Bristow, Dorothy M. Broomfield, Gillian L. Browne, Shirley D. Campbell, J. J. Cockburn, Patricia M. Conroy, K. J. Cowen, Patricia J. Dockery, F. O. Dosekun, J. H. N. Ferris, W. T. J. Gogan, M. K. Hay, Patricia C. Hodson, Janet Hogan, Barbara Holmes, M. G. D. Hurly, Dorothy I. Jones, R. C. Keays, J. J. Kevany, E. F. Lavelle, A. D. McGugan, Laura Maslin, Kathleen M. Muirhead, C. C. C. O'Morchoe, C. J. B. Orr, J. D. Page, W. Pollard, Patricia J. Richardson, H. W. P. Rooke, J. A. Scott, A. W. C. Stewart, I. J. Temperley, G. A. Weaver, C. D. Whitfield, Jean Williamson, T. J. Woods, L. Zimich.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

On July 7 Mr. A. Lawrence Abel was re-elected and Mr. R. H. O. B. Robinson and Mr. Harold C. Edwards were elected members of the Council of the College. The result of the poll was as follows:

Elected	*Votes*
Arthur Lawrence Abel (Princess Beatrice Hospital) ..	911
Harold Clifford Edwards (King's College Hospital) ..	864
Ronald Henry Ottywell Betham Robinson (St. Thomas's Hospital)	836

In all 2,118 Fellows voted; in addition 20 votes were found to be invalid.

At a meeting of the Council of the College held on July 14 the Hallett Prize was awarded to Dr. B. J. Dooley (Melbourne), and Dr. Angus Macpherson was re-elected Laming Evans Research Fellow for a third year from August 1, 1955.

A diploma of Fellowship was granted to W. A. Malik (Punjab).

The Council agreed to a number of measures designed to facilitate the arrangements for reciprocity of Primary Fellowship examinations with other colleges of surgeons.

Professors and Lecturers for the ensuing year were appointed as follows:

Hunterian Professorships.—Dr. E. Rohan Williams, one lecture on the skull at birth; Mr. Ashton Miller, one lecture on diverticulum of the bladder, with particular reference to aetiology and treatment; Mr. Eric Samuel, one lecture on the anatomy of the bile ducts in relation to the post-cholecystectomy syndrome; Mr. D. M. Wallace, one lecture on the natural history and possible cause of bladder tumours; Mr. S. S. Anand, one lecture on hypertrophic ileo-caecal tuberculosis in Indian patients; Mr. J. H. Peacock, one lecture on the aetiology, diagnosis, and treatment of Raynaud's disease, Raynaud's phenomenon, and acrocyanosis in the upper limb; Mr. B. B. Milstein, one lecture on cardiac arrests and resuscitation; Mr. F. T. Graves, one lecture on the anatomy of the intrarenal arteries in health and disease; Mr. J. S. R. Golding, one lecture on bone changes in sickle-cell anaemia; Mr. Leon Gillis, one lecture on amputations in children; Mr. B. Mukopadhaya, one lecture on the role of excisional surgery in the treatment of bone and joint tuberculosis; Mr. E. F. Chin, one lecture on the surgery of funnel chest and pigeon chest; Mr. C. W. D. Lewis, one lecture on melanomas and melanosis; Mr. W. J. W. Sharrard, one lecture on the muscle paralysis in poliomyelitis; Mr. Charles Marks, one lecture on observations on the surgical sequelae of bilharzial disease.

Arris and Gale Lectureships.—Dr. F. Dudley Hart, one lecture on hormone replacement therapy in the surgery of endocrine disorder; Dr. Roger Warwick, one lecture on the functional topography of oculomotor nuclei; Dr. J. D. Griffiths, one lecture on the surgical anatomy of the blood supply of the distal colon.

Erasmus Wilson Demonstratorships.—Dr. B. E. Heard, two demonstrations; Dr. J. S. Young, one demonstration; Dr. L. M. Franks, one demonstration; Mr. L. W. Proger, two demonstrations.

Arnott Demonstratorships.—Professor G. W. Causey, one demonstration; Professor David Slome, one demonstration; Dr. Frank Stansfield, one demonstration; Professor R. J. Last, one demonstration; Dr. R. McP. Livingston, one demonstration; Miss Jessie Dobson, one demonstration.

Vital Statistics

OUTBREAK AT ROYAL FREE HOSPITAL

OBSCURE NATURE OF INFECTION

The following information has been received from the Royal Free Hospital:

During the past four weeks 83 of the nursing staff, 5 of the medical staff, 11 of the ancillary medical staff, 8 of the students, and 22 of the domestic staff of the Royal Free Hospital at Gray's Inn Road and Liverpool Road, London, have developed an infection. Initially, the cases were referred to as glandular fever, but, as the outbreak has progressed, so many unusual features have been observed that it is now difficult to use that, or any other, diagnostic label. Lymph nodes, liver, and spleen are involved, and a large majority of the cases show signs and symptoms of encephalomyelitis or polyneuritis. The disease has usually run a benign course.

The incubation period appears to be five to seven days. Although the majority of patients were young nurses, some were sisters, and some of these are over 40 years of age. The initial symptom has been vague malaise, followed within one to about seven days by mild sore throat; tender enlargement of the lymph glands, often confined to the posterior cervical region, but in some cases generalized; pain under both costal margins and in the neck, back, and limbs of varying severity. Headache without meningism has been common, but the symptom which seems to be peculiar to this infection, especially in the early stages, is vertigo. This has often been transient, but in a few cases it has been persistent and severe, and has been accompanied by slight nerve deafness.

Symptoms and signs of encephalomyelitis have appeared in some cases within 48 hours of the onset, but in others these neurological complications have been delayed for as long as three weeks. Cranial nerve pareses, particularly ocular, have been common; mild paresis of either pyramidal or lower motor neurone type has been observed, sometimes with painful muscle spasms. Paraesthesia, numbness, neuralgic pains, or anaesthesia have appeared either alone or in association with motor manifestations. Coma was not observed, but a state of drowsiness has been relatively common.

Tenderness of the lymph nodes has been accompanied in some cases by extreme tenderness in the region of the liver and over the spleen. Liver enlargement has been quite definite, but tenderness has made it difficult to determine the size of the spleen. Even when the infection has been severe, pyrexia has been slight or absent. In certain cases there has been a disproportionate tachycardia, sometimes persisting into convalescence.

Haematological investigations have revealed total white cell counts varying from 3,000 to 12,000 per c.mm., sometimes with a neutropenia and occasionally with an absolute lymphocytosis. Although typical glandular fever cells have not been observed, morphological changes have occurred in some lymphocytes, and the specificity of these is being studied. The Paul–Bunnell test has not been found to be positive in any case. The cerebrospinal fluid has been examined in a few cases, and in none was there a pleocytosis or an increase in the protein content. With the help of a number of virus workers outside the hospital extensive studies are being made to identify the aetiological agent.

On clinical grounds it seems doubtful if this is an outbreak of infectious mononucleosis, for, though the neurological complications encountered in the present outbreak have been described in reports of that disease, they were exceptional in other epidemics: yet in the present epidemic they are almost the rule. Furthermore, laboratory tests at the hospital have failed to support a diagnosis of infectious mononucleosis. On the other hand, it is known that in the "epidemic variant" of infectious mononucleosis haematological and serological changes typical of the

classical disease are less constant. The very high infectivity, the prominence of visceral manifestations, the frequency of sensory neurological signs, combined with the predominantly benign course make a diagnosis of polioencephalitis most unlikely. The studies in progress may establish that the infection is due to a known virus or its variants, but it is possible that a new virus is involved.

Poliomyelitis in England and Wales

The incidence of acute poliomyelitis so far this year is about average for the years since the war. An unusually high proportion of the cases are non-paralytic. In the week ending July 30, 241 cases were notified. Of these, 121 were paralytic and 120 non-paralytic. The total is an increase of 64 over the total for the previous week.

From the beginning of the year to July 30, 1,213 cases had been notified. This total may be compared with 986 in 1954, 1,959 in 1953, 1,430 in 1952, 1,282 in 1951, 2,226 in 1950, 1,016 in 1949, 830 in 1948, and 1,142 in 1947. Deaths in the 160 great towns numbered 2. From the beginning of the year to July 30, 37 had been reported, as compared with 35 in 1954 and 111 in 1953.

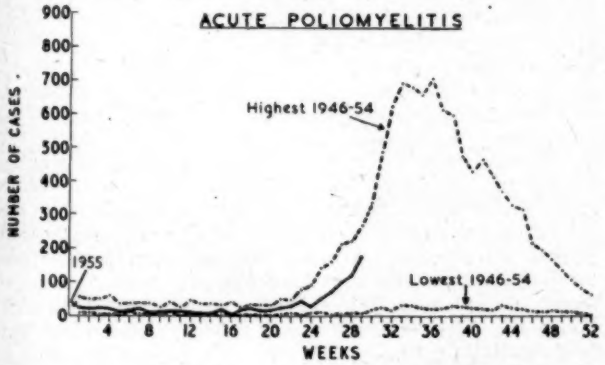
The important centres of the disease so far have been Barnsley C.B. in Yorkshire, and Stepney M.B., London. By July 30 notifications this year in Barnsley had reached the total of 61, and in Stepney 33, giving rates per 100,000 of 81 and 34 respectively. In Willesden M.B. 36 cases of non-paralytic disease (none of paralytic) were reported in the fortnight ending July 30.

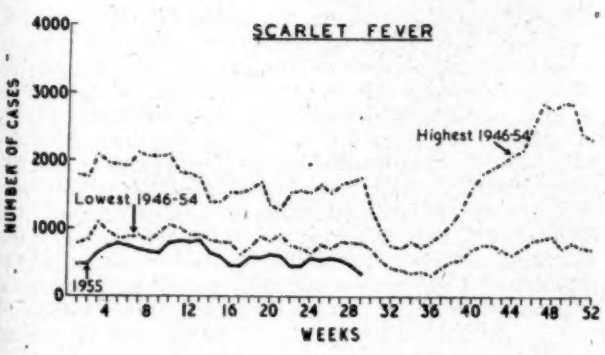
Week Ending July 30

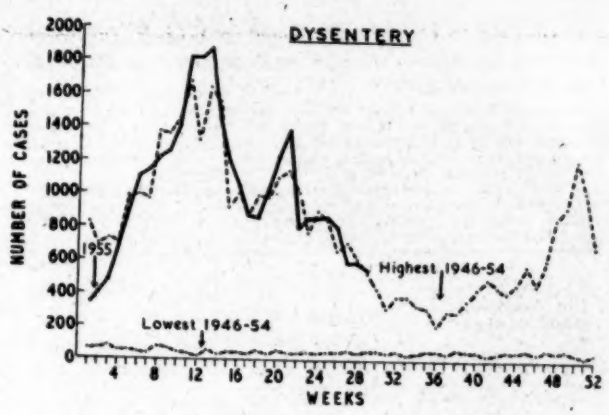
The notifications of infectious diseases in England and Wales during the week included: scarlet fever 342, whooping-cough 1,705, diphtheria 7, measles 12,100, acute pneumonia 233, acute poliomyelitis 241, dysentery 471, paratyphoid fever 29, and typhoid fever 6.

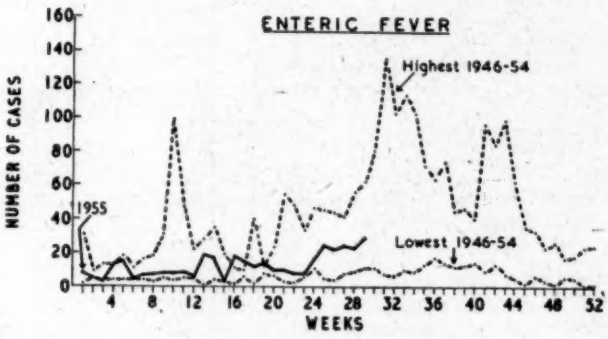
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1946–54 are shown thus ------, the figures for 1955 thus ———. Except for the curves showing notifications in 1955, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

The incidence of measles and dysentery continued to decrease in England and Wales in the week ending July 23, but notifications of several other infectious diseases rose. Notifications of pneumonia increased by 16 from 232 to 248, of acute poliomyelitis by 57 from 120 to 177, and of whooping-cough by 28 from 1,760 to 1,788. Notifications of measles fell by 1,889 from 16,425 to 14,536, of dysentery by 48 from 596 to 548, and of scarlet fever by 108 from 460 to 352. 20 cases of paratyphoid and 9 of typhoid fever were reported, these being 4 more and 2 more respectively than in the previous week.

The largest declines in the incidence of measles were 111 in Devon, from 704 to 593, 124 in Durham, from 387 to 263, 91 in Hertfordshire, from 431 to 340, 219 in Leicestershire, from 637 to 418, 267 in Middlesex, from 807 to 540, and 120 in Northumberland, from 227 to 107. The cases of enteric fever were widespread; Devon reported 2 of typhoid (Exeter C.B. 1, Okehampton R.D. 1), Lancashire 4 of typhoid (Liverpool C.B. 3, Lancaster M.B. 1), London 3 of paratyphoid and 1 of typhoid, Northumberland 1 case of each, Surrey 2 of paratyphoid (Caterham and Warlingham U.D. 1, Egham U.D. 1), and Yorkshire West Riding 6 of paratyphoid (Dewsbury C.B. 3, Sheffield C.B. 2, Brighouse M.B. 1).

The largest returns of dysentery were from Lancashire 188 (Blackpool C.B. 39, Liverpool C.B. 60, Ashton-under-Lyne M.B. 21), and Yorkshire West Riding 79 (Huddersfield C.B. 31, Leeds C.B. 31).

In Scotland 213 cases of dysentery were notified, being 45 more than in the previous week. The largest return was Glasgow 114.

Venereal Diseases

In England and Wales during the quarter ending March 31, 1955, 1,247 new cases of syphilis were reported as attending the clinics. Of these, 205 were classified as primary, secondary, or latent in the first year of infection. 10 cases of congenital syphilis in children aged under 1 year were reported, and 171 cases in persons over that age. New cases of gonorrhoea numbered 3,657, of chancroid 69, and of non-gonococcal urethritis (males only), 2,920.—*Monthly Bulletin of the Ministry of Health*, July, 1955.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **July 23** (No. 29) and corresponding week 1954.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	8	2	3	0		13	1	8	0	0
Dysentery	548	46	213	20	1	534	96	210	8	1
Encephalitis, acute	1	0		0		7	2	0	0	
Enteric fever:										
Typhoid	9	1	1	0		3	2	0	0	0
Paratyphoid	20	3	3	0		9	0	0	0	0
Food-poisoning	450	103		4		221	22		15	0
Infective enteritis or diarrhoea under 2 years				17	19				18	15
Measles*	14,536	192	64	95	77	2,965	169	62	110	144
Meningococcal infection	34	7	12	2		31	3	14	1	0
Ophthalmia neonatorum	35	3	10	0		22	3	14	0	
Pneumonia†	248	9	95	2	6	254	15	108	2	2
Poliomyelitis, acute:										
Paralytic	93	15	12	0	1	56	1	20	2	2
Non-paralytic	84	20				35	3			
Puerperal fever§	234	38	9	0		245	48	17	1	0
Scarlet fever	352	23	26	9	8	785	45	78	18	17
Tuberculosis:										
Respiratory	715	99	98	36		781	77	133	39	
Non-respiratory	98	6	19	3		104	4	14	3	
Whooping-cough	1,788	91	64	53	108	2,030	112	155	22	18

DEATHS in Great Towns	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	0	0		1		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	6	0	1	1	2	3	0	0	0	0
Influenza	1	0	0	0	1	5	1	0	0	0
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	1				0	1		
Pneumonia	156	18	6	5	5	133	24	16	5	4
Poliomyelitis, acute	1	0			0	1	0			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	57	9	9	1	6	59	6	10	1	2
Non-respiratory		2	2	0	1		3	11	0	1
Whooping-cough	0	0	0	0	0	1	0	0	0	0
Deaths 0–1 year	188	22	19	5	14	183	14	25	6	7
Deaths (excluding stillbirths)	4,235	656	553	88	125	4,396	650	569	83	146
LIVE BIRTHS	7,562	1193	952	262	388	7,420	1080	970	218	400
STILLBIRTHS	203	28	25			175	23	27		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia

Medical News

How to Help Medical Charities.—A pamphlet giving details of the Royal Medical Benevolent Fund, the Royal Medical Foundation of Epsom College, the Royal Medical Benevolent Fund Society of Ireland, the Sir Charles Hastings Fund, the Christine Murrell Fund, and the Dain Fund—and how most helpfully to subscribe to them—has been printed, and may be obtained on request to the Secretary, B.M.A. House, Tavistock Square, London, W.C.1. The pamphlet contains an earnest appeal that all medical men and women should subscribe to one or more of these charities.

Rockefeller Munificence.—Rockefeller grants for the second quarter of 1955 exceeded 5.6 million dollars. Their range and imaginative conception are equally on the grand scale. There are four major benefactions to medicine, two of which are to support British work: $848,600 for the development of five medical schools in South America; a five-year grant of $314,000 for the medical faculty of the University College of the West Indies, Jamaica, to help expand the research and teaching programme based on the study of local diseases and health problems; $156,000 for laboratory facilities at Oxford for the new Regius Professor of Medicine, Professor G. W. PICKERING; and $150,000 to support a long-term study of respiratory-disease viruses by the director of the Division of Interepidemic Ecology at the School of Hygiene and Public Health, Johns Hopkins University. Other grants for medical projects go to such diverse undertakings as the Nurse Teaching Unit at Edinburgh (see paragraph below); the planning of a State-wide health and medical care programme for North Carolina; a study of the nature of "hybrid vigour" by Dr. D. C. WARREN at Purdue University, Indiana; a headquarters building for the Indian Council of Medical Research; the establishment of a register of hereditary diseases at the Oslo Institute of Genetics; the support of research workers with equipment, funds, or opportunities for travel; and the costs of a Sabbatical year at Oxford for an American professor of physiology. Some of the other grants in the quarter's list, while not strictly medical, are of interest: the dean of admissions and financial aids of Harvard University has a grant to study "college and university admission policies in Great Britain"; there is a grant for a New York University worker for a study of the legal problems of the Welfare State, the work to be done at Oxford; another for a study of adjustment during the middle years of marriage, by Professor E. W. BURGESS, of Chicago University. The Massachusetts Institute of Technology receives a grant to support a journal devoted to the translation of languages with the aid of machines; one of the editors of *Nature* goes to America to confer with editors and authors of scientific publications in the United States. Finally, mention must be made of two substantial grants to two British universities: $30,000 to University College, London, to support Professor L. S. PENROSE'S research on human genetics, and $21,000 to Queen's University, Belfast, to support research on viruses by Professor G. W. A. DICK.

Nurse Teaching Unit at Edinburgh.—In its quarterly report the Rockefeller Foundation announces a five-year grant of £30,000 for the establishment of a Nurse Teaching Unit at Edinburgh University, which would be the first of its kind to be formed within the framework of a British university. The grant was reported to the Court of Edinburgh University at its meeting on July 18, and it is understood that a committee is now considering the establishment of the unit and will make recommendations through the Medical Faculty and Senate. The object of the Unit, according to the Rockefeller Foundation, would be to prepare teachers and administrators in the nursing profession with the ultimate aim of providing a "regular supply of well-trained nurses to meet the changing needs in nursing

education and services." For the past ten years the Royal College of Nursing in Scotland has organized post-registration courses for nurses, particularly those entering teaching, the University of Edinburgh providing the teachers, setting the examinations, and awarding the certificates. The content of the course was recently reviewed by Miss G. B. CARTER, while holding a Boots Research Fellowship in Nursing, and improvements were suggested. The present offer on the part of the Rockefeller Foundation follows a visit of their nursing adviser, Miss M. E. TENNANT, to Edinburgh.

Sir Earle Page, Chancellor of New University.—Sir EARLE PAGE, Federal Minister of Health of Australia and former surgeon, was installed as the first Chancellor of the University of New England at Armidale, New South Wales, on August 4. He had been chairman of the council of the New England University College, the predecessor of the new university, since its inception in 1938 as a branch of Sydney University, Armidale being 350 miles distant. Autonomy was granted early in 1954, and at present there are Faculties of Arts and Science. Faculties of Agriculture and Agricultural Economics are contemplated. A feature unique among Australian universities is that all students, unless married or living with their parents or legal guardians, must be residential.

R.S.I. Becomes Royal Society for the Promotion of Health.—The Royal Sanitary Institute announces that in future it will be known as the Royal Society for the Promotion of Health. The change in title, after approval by the Queen, patron of the Institute, was unanimously adopted at a recent Extraordinary General Meeting of members, under the chairmanship of Sir ARTHUR MACNALTY. The official announcement states that the word "sanitary" has now become a misnomer, the scope and work of the Institute comprising all aspects of health, not being confined to any particular branch of it. The Institute was founded in 1876 for the purpose of promoting the health of the people. Now there are over 12,500 members, branches in Australia, New Zealand, and South Africa, and 20 overseas examination boards. The first Fellows included Sir Edwin Chadwick, Sir Benjamin Ward Richardson, and Florence Nightingale. Current activities of the Society are modernization of the Museum of Health, and plans for some fresh features at next year's congress.

Royal College of Physicians: Orator and Lecturers.—Professor J. CRIGHTON BRAMWELL was appointed Harveian Orator and Dr. W. PHILLIPS Bradshaw Lecturer for 1956 at the quarterly comitia on July 28. The following lecturers for 1956 were also appointed: Lumleian, Dr. F. AVERY JONES; Goulstonian, Dr. J. R. ELLIS; Oliver-Sharpey, Professor A. C. FRAZER; Lloyd-Roberts, Sir MAURICE BOWRA; Bertram Louis Abrahams, Dr. I. DE B. DALY, F.R.S.; Humphry Davy Rolleston, Professor F. T. G. PRUNTY. For 1957 the following lecturers were appointed: Croonian, Professor G. W. PICKERING; FitzPatrick, Dr. C. F. T. EAST; Watson Smith, Dr. R. M. B. MACKENNA.

Marc Daniels Memorial Lecture.—Mr. and Mrs. DANIELS have given to the Royal College of Physicians and the Medical Research Council a donation to found a lecture in memory of their son, Dr. MARC DANIELS, who died in March, 1953, aged 46. Dr. Daniels is remembered particularly for the important part he played in organizing the various Medical Research Council trials on the treatment and prevention of tuberculosis. The first lecture will be given by Sir GEOFFREY TODD on January 12 next year.

Notes on Atomic Energy for Medical Officers.—Her Majesty's Stationery Office has published a 170-page illustrated Admiralty booklet entitled *Notes on Atomic Energy for Medical Officers* (price 6s. net). Prepared by the staff of the Royal Naval Medical School, Alverstoke, the *Notes* aim to provide medical officers with the necessary basic facts for an understanding of the immediate and late consequences of atomic explosions and the hazards of radiation warfare generally. Starting with elementary physics and atomic structure, the book proceeds to describe the release of atomic energy and the properties of fission products. Then follow chapters on the effects of radiation on the body, monitoring and protection, and the treatment of radiation casualties.

Baly Medal.—Professor A. L. HODGKIN, F.R.S., research professor of the Royal Society, has been awarded the Royal College of Physicians' Baly Medal for 1955. The award is for his "services to physiology and his work on the conduction and excitation of nerve fibres and the biophysics of the cell membrane."

Aberdeen University.—Dr. H. W. KOSTERLITZ, lecturer in physiology, and Dr. T. N. MORGAN, lecturer in materia medica, have been appointed readers.

Wellcome Foundation.—The Wellcome Trustees announce the appointment of Brigadier J. S. K. BOYD, F.R.S., as a Trustee, as from January 1, 1956, in succession to Professor T. R. ELLIOTT, F.R.S., who is retiring in October. Brigadier Boyd is relinquishing the directorship of the Wellcome Laboratories of Tropical Medicine on December 31, and will be succeeded by Dr. R. S. F. HENNESSEY, lately Director of Medical Services, Uganda.

Methylpentynol has been added to Part I of the Poisons List and to the First Schedule to the Poisons Rules.

Dr. W. S. C. Copeman, chairman of the Empire Rheumatism Council, is going to Australia and New Zealand for a lecture tour. He will be away about four months.

COMING EVENTS

British Association for the Advancement of Science.—The 117th annual meeting will be held at Bristol from August 31 to September 7 under the presidency of Sir ROBERT ROBINSON, O.M., F.R.S.

Lectures for Medical Photographers.—Details of a series of 12 lectures for medical photographers at the Polytechnic, Regent Street, London, W.1, may be obtained from Miss J. HUNT, The Royal Marsden Hospital, Fulham Road, London, S.W.3. The course begins on September 28, but application for admission should be made immediately. The fee is £1.

Minnesota Symposium on Arteriosclerosis.—An international symposium on arteriosclerosis, under the chairmanship of Dr. ANCEL KEYS, will be held at the University of Minnesota Medical School, Minneapolis, 14, Minnesota, from September 7 to 9.

NEW ISSUES

Abstracts of World Medicine.—The August issue (Vol. 18, No. 2), which is now available, contains abstracts of important papers drawn from medical and other scientific journals published in some 20 different countries and in all five continents. The subjects covered range over the whole field of clinical medicine, and include pathology, bacteriology, pharmacology, and chemotherapy; there are also sections dealing with medical genetics, public health and industrial medicine, forensic medicine and toxicology, anaesthetics, radiology, and the history of medicine. Issued monthly; annual subscription £4 4s.; single copy 8s. 6d.; a specimen will be sent free on request to the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Abramson.—On July 16, 1955, at Ayrshire Central Hospital, Irvine, to Morag (formerly Dods), M.R.C.O.G., wife of Dr. Allan Abramson, 6, Whinfield Road, Prestwick—a son.

Minto.—On July 16, 1955, at Carlisle, to Dorothy (formerly Crais), wife of W. H. P. Minto, M.D., D.P.H., Croft House, Brampton, Cumberland, a third son.

DEATHS

Cameron.—On July 18, 1955, at "Ardmore," Crosthwaite Road, Keswick, Cumberland, John Cameron, M.B., Ch.B., aged 47.

Chalmers.—On July 21, 1955, Joseph Chalmers, M.B., Ch.B., D.P.H., of Oaklands House, Keighley, Yorkshire.

Doggart.—On July 21, 1955, at 10, Church Lane, Walthamstow, E.17, Ann McC. Black Doggart, M.B., Ch.B.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Does Freezing Sterilize Water?

Q.—*How resistant are typhoid and dysentery organisms to freezing? Is ice made with unboiled water from a doubtful supply safe to use in drinks?*

A.—The short answers to these questions are "Very" and "No." It is a common mistake to suppose that cold is lethal to bacteria. There are a few species—not including any of the intestinal pathogens—which are unable to tolerate cold under certain conditions, but for the great majority it does no more than arrest growth, and in this state they survive for longer than at higher temperatures. As an example of innumerable observations on the prolonged survival of bacteria at low temperatures reference may be made to those of M. J. Prucha and J. M. Brannon,[1] who introduced typhoid bacilli into ice cream and kept it frozen hard for over two years. The bacilli survived in slowly diminishing numbers throughout this time.

REFERENCE

[1] *J. Bact.*, 1926, **11**, 27.

Kymography versus Air Insufflation: Risks where Infection is Present

Q.—*Will your expert kindly tell me the advantages and disadvantages of a portable kymograph over a simple air insufflation apparatus such as Bonney's? I am working in an area of Africa where the incidence of gonorrhoea is high and sterility the commonest gynaecological complaint. Would it be safe, in the absence of obvious vaginal infection, to carry out tests of tubal patency under penicillin cover?*

A.—The advantages claimed for any type of kymograph as compared with a simple insufflator are: (i) A permanent record of the findings is obtained. (ii) The tracing shows a contraction pattern which is said to reflect not only tubal patency and cornual spasm but tubal disease such as hypoplasia, fibrosis, stenosis, and peritubal adhesions. (iii) The use of carbon dioxide not only provides for more rapid absorption from the peritoneum, but, if it enters the blood stream, does not result in serious embolic consequences because of its high solubility. The first argument is of little importance and the second is supported by enthusiasm rather than by scientific data. Indeed, it has been shown fairly conclusively that the kymograph "waves" do not represent tubal contractions and that their particular pattern bears no relation to tubal lesions as found at simultaneous laparotomy, nor to the patient's subsequent fertility.

It is the safety of carbon dioxide from the standpoint of embolism which is the chief advantage of the kymograph. There are many recorded fatalities from air embolism using simple insufflation apparatus, but—and this is the point usually overlooked—the risk of embolism depends on the amount of air injected, and it is reckoned to require more than 100 ml. for a fatal result. Nearly all fatalities have occurred when a large capacity bulb, or one fitted with a valve which allows it to be filled and emptied several times (for example, the bulb of the sphygmomanometer) has been used. The bulb of Bonney's apparatus has a capacity of only 80 ml., and it has no valve, so that it is impossible to inject a fatal dose of air if the proper technique is observed. There are hospitals in Britain where many thousands of air insufflations with the Bonney's apparatus have been carried out without a single case of fatal or even clinically recognizable air embolism.

The kymograph also has disadvantages. Its complicated nature makes it less dependable, and its many joints are subject to leaks which, if they occur within the machine, are not easily recognized and produce a tracing similar to that of a normal positive patency test. Moreover, the machine itself cannot be sterilized, so that gas is delivered along a potentially septic pathway for part of its course. It may be added that, unless all the tubing is first flushed with gas as a preliminary step, it is air which first enters the uterus and tubes.

It may be concluded, therefore, that the appeal of the kymograph is a rather superficial one, and that, despite statements to the contrary, air insufflation from the Bonney apparatus is not specially dangerous, *provided that the proper valveless bulb is employed*, and provided that the usual precautions are taken. Moreover, as compared with the kymograph, it has the advantages of simplicity, cheapness, sterility, and reliability.

Salpingitis is a complication of insufflation in approximately 0.5% of cases, and occurs irrespective of the type of apparatus used. Lower estimates of this risk are given, but they are probably optimistic. However, it is now fairly well established that such salpingitis does not usually result from blowing pathogenic organisms from the vagina and cervix into the tubes but represents an exacerbation of a previously present chronic salpingitis (which is sometimes tuberculous). It is important, therefore, to avoid insufflation when there is evidence of active or recently active salpingitis or any feature suggesting pelvic tuberculosis. It is nevertheless obviously unwise to carry out the test in the presence of active infection in the lower genital tract. The vagina always contains organisms of some kind, so preoperative cultures are of little value. A precaution which might be taken is to examine vaginal swabs for pus cells, which, if present in significant numbers, generally indicate active infection. A penicillin "cover" might have a place in the circumstances described, but is not generally used.

Insufflation can be carried out as an out-patient procedure, and indeed this is the general practice. The avoidance of hospitalization is convenient for both patient and hospital. Nevertheless, it probably means a lower standard of asepsis, more discomfort to the patient, and probably more likelihood of tubal spasm vitiating the result. Without anaesthesia the cannula of Bonney's apparatus cannot usually be used because it requires preliminary dilatation of the cervix; however, it can be replaced by a smaller one of the Rubin pattern. It should be noted, too, that instrumentation of the endocervix and insufflation occasionally induce a severe and alarming state of shock in the unanaesthetized woman.

Surgery in Parkinson's Disease

Q.—*What place has destruction of the globus pallidus in the treatment of Parkinsonism? Recent American reports describe both ligation of its blood supply and alcohol injection.*

A.—Surgery has no place, at the present time, in the treatment of the majority of patients suffering from Parkinson's disease. However, where the disability occasioned by tremor and rigidity is very severe, and particularly where the disturbance is predominantly unilateral in relatively young patients, the possibility of surgical alleviation merits consideration. In the past many thought that, if operation was to bring relief, paralysis must be produced by either cerebral cortical excisions or section of the pyramidal tracts in the cord. However, following accidental occlusion of the anterior choroidal artery, a patient operated on by I. S. Cooper was completely relieved of Parkinsonian tremor and rigidity. Cooper subsequently deliberately occluded this vessel in 34 patients, and claims considerable relief of disability with reduction of tremor and rigidity in a high proportion of cases.[1] The great advantage of this form of surgery, which devascularizes the globus pallidus, is that it relieves the abnormal tone and rigidity without producing paralysis. If wider experience and observation of cases over a longer post-operative period confirm the early results recorded, occlusion of the anterior choroidal artery will mark

a definite advance in the treatment of cases of severe Parkinsonism. The more recent introduction of chemo-pallidectomy[2] is an attempt to destroy the globus pallidus by the injection of alcohol into it. The procedure was introduced in the hope of bringing within the range of active treatment patients who are considered too old—that is, over 55 years—to be submitted to the more severe operation of occlusion of the anterior choroidal artery. The early results reported have been encouraging, but it will be some years before the value of either procedure can be accurately assessed.

REFERENCES
[1] *J. Amer. geriat. Soc.*, 1954, **2**, 691.
[2] *Science*, 1955, **121**, 217.

Validity of Urine Alcohol Estimations

Q.—*How accurately does the urine alcohol level reflect the blood level? I notice that it is stated in the B.M.A. pamphlet on "The Recognition of Intoxication" (1954) that, in legal cases, urine samples are as satisfactory as blood samples for alcohol estimations, besides being easier to collect.*

A.—The alcohol in the urine is in equilibrium with that in the blood and the ratio of the two is constant irrespective of the rate of urine secretion. The urine concentration will therefore reflect accurately the average blood concentration during the intervals between emptying the bladder. It therefore gives much the same information as a single blood estimation taken at the same time as the patient empties his bladder. A completely accurate assessment can be made only on a full blood alcohol curve such as is carried out in experimental subjects. The blood alcohol is therefore no "fairer" than a urine estimation.

Early Breast Development

Q.—*A relation of mine is worried because the breasts of her daughter show distinct signs of development at the age of just 7 years. Can I reassure my relative that this is normal, or should I risk having the child's attention unduly focused by advising specialist consultation? There are no other signs of approaching puberty. The child appears perfectly normal in every other way. She is of slight build.*

A.—Breast development is one of the first signs of puberty and is usually noticeable in the form of the "areolar bud" by the age of 9 or 10 years, and even before this there may be slight deposition of fat. Significant enlargement at the age of 7 years is unusual but not rare, and if development proceeds without change of pace it probably means that menstruation will begin by the age of 9 or 10 years. There is no need for alarm, however, because precocious puberty is "constitutional" in 90% of cases. That is, it represents an individual characteristic and has no pathological significance.

In this case it might be wise for the lower abdomen to be examined to exclude the remote possibility of a granulosa cell tumour of the ovary. In the absence of obvious sign of such, however, it is probably best to do nothing except await developments, for if the precocious development is constitutional no treatment is indicated.

Unilateral Cryptorchidism in a Boy

Q.—*What treatment is advised for a boy of 14 in whom only one testicle has descended into the scrotum? What is the prognosis as regards fertility?*

A.—If the changes of puberty have already begun, the failure of testicular descent on one side strongly suggests ectopia, for which only surgery can be effective. The reason for advising treatment at this stage, however, can be only cosmetic or the fear that the ectopic testis is more likely to become the site of neoplasia. So far as sperm production is concerned, the testis must be regarded as irretrievably damaged as a result of its not having entered the scrotum before the onset of puberty. If, on the other hand, puberty has not yet begun, it would be reasonable to try treatment with chorionic gonadotrophin—for example, 1,000 I.U. twice weekly for 10 weeks. Failure to descend by the end of this course would indicate the necessity for urgent surgery. If undertaken in time, this might prevent the germinal destruction which would otherwise certainly follow failure to descend into the scrotum before puberty.

The prognosis as regards fertility is undoubtedly impaired in patients with unilateral cryptorchidism, since there is commonly an accompanying testicular dysplasia affecting even the descended testis. On the other hand, in some of these patients the descended organ is perfectly normal, and then the prognosis as regards fertility is excellent. It is likely to be influenced by treatment only in so far as, by bringing down the undescended organ before puberty, this testis is given a chance to produce spermatozoa. If there is congenital testicular dysplasia as well, treatment can be expected to achieve little or nothing.

Delay in Completion of Immunization Injections

Q.—*The interval between injections for prophylaxis against diphtheria, whooping-cough, etc., is recommended as one month. If the second or third injection has to be postponed, say for another month, on account of intercurrent illness, is it necessary to start the series of injections at number one again, or is the longer interval unimportant regarding the immunity conferred?*

A.—This depends to some extent on the type of prophylactic used and the age at which immunization is started.

In combined immunization of young babies with a diphtheria–pertussis prophylactic, it is important to ensure that too long an interval is not left between the first two doses. This is particularly the case if the first dose is given before the baby is 3 months old, as there may be interference with the action of the dose in some babies, by maternally conferred antibodies. An interval of two months between the first two injections would be satisfactory in most cases. If more than two months elapse, it would appear to be safer to start the course again. The interval between the second and third doses is less important, and it is probable that it could be extended to three or four months if the first two injections had been given at the recommended times.

In immunization against diphtheria, using a dosage of 0.5 ml. of A.P.T. or P.T.A.P., an interval of two to three months between the first two doses would certainly not be excessive, so long as immunization was not started at a very early age. It is indeed advantageous to give the doses of such prophylactics separated by an interval of longer than a month.

Hiccup during Anaesthesia

Q.—*What is the reflex arc responsible for the production of hiccup? As hiccup is said to be associated with acidosis and carbon dioxide accumulation, why is it that the inhalation of 5% carbon dioxide often stops an attack? I am interested especially from the anaesthetist's point of view.*

A.—Hiccup is a reflex, the efferent pathway of which is the phrenic nerve. The initiation of the reflex may arise from a number of sites, of which the gastric mucosa, the alimentary canal, the peritoneal cavity, the diaphragm, and the respiratory centre itself are examples. The afferent pathway therefore varies according to the aetiological circumstances. As with other reflex phenomena which arise from a variety of different sites and stimuli, it is unwise to transfer observations regarding one arc to circumstances in which another operates. The inhalation of carbon dioxide mixtures often stops hiccup, and in these circumstances it is unlikely that acidosis is present as a precipitating factor. Hiccup is rarely a feature of conditions (for example, diabetes) in which acidosis is present. During the course of anaesthesia hiccup is generally evidence of insufficient anaesthesia—that is, insufficient depression of reflex irritability, or evidence of insufficient curarization. Hiccup is therefore terminated by increasing the depth of anaesthesia—that is, by the administration of depressants (whether these

be ether, thiopentone, or procaine), or by increasing the extent of curarization by the administration of further doses of relaxant. The administration of carbon dioxide, methylamphetamine, ammonia, and other drugs may be effective, because they initiate effects which occupy some part of the reflex pathway of the hiccup reflex.

Measuring the Danger of Exposure to Benzene

Q.—*Can you give me any information about the urine sulphate test and its application to the detection of recent exposure to benzene? I have read that the ratio of inorganic sulphates to total sulphates is a direct measure of recent benzene exposure, with the following data:*

Urine Sulphate Ratios	*Benzene Exposure*
75%–90%	None
50%–75%	Slight
25%–50%	Unsafe
0%–25%	Dangerous

Can you tell me how the total sulphate estimation is done?

A.—The urine sulphate test gives a measure of "benzene exposure" and may be used as a warning signal of dangerous concentrations of the vapour breathed. Urine sulphate ratio is the amount of inorganic sulphates in the urine divided by the amount of total sulphates; it gives a measure of the amount of benzene vapour absorbed by the individual during the working period immediately prior to the test; and it gives a definite warning signal of danger before chronic poisoning results and the health of the individual is affected. The test has no diagnostic value and tells nothing about the health of the individual at the time the test is made. It is not a measure of benzene poisoning and should not be used as a measure of blood damage. The method for estimating total sulphate is described in *Practical Physiological Chemistry* by Hawk, Oser, and Summerson, 12th edition, 1947 (Blakiston, Philadelphia), p. 884 *et seq.*

NOTES AND COMMENTS

Progressive Asthma.—Dr. J. MAIZEL (Whitwell, Notts) writes: Referring to your note in "Any Questions?" (July 2, p. 73) about progressive asthma, it seems to me that undue recourse to corticotrophin for relief can be as dangerous as morphine injections. I assume that the patient in question has been already investigated regarding any chronic infection. The emotional aspect of asthma does not seem to have been considered, yet it is always present in varying degrees. In progressive asthma the patient has often lost a grip on the situation, and so a vicious circle of apprehension and tension results. Medical hypnosis, by a specialist in this branch of therapy, is a much safer method of control and well worth a trial.

OUR EXPERT replies: Medical hypnosis in individual patients and in expert hands sometimes helps, but usually only temporarily. It is not a method of therapy which at present commands general support. An emotional aspect in asthma is indeed often common, as is suggested, but I cannot agree that it is *always* present. In this particular patient, a woman of 26 years, the history was that so often found when infection is the dominant cause of the asthma (for which further investigation and possible treatment was advised), and there was no suggestion given by her doctor-husband of any possible psychogenic factor.

It is, of course, agreed that morphine is dangerous in asthma (paraldehyde was advised instead) and that *undue* recourse to corticotrophin is also dangerous, but in quite a different way. It is the overlooking of accepted contraindications, and lack of care in avoiding complications, which make it dangerous. Corticotrophin given with proper regard to its contraindications (peptic ulcer, tuberculosis, unstable personality, diabetes, and hypertension), and in proper dosage, can bring temporary relief to over 80% of patients in status asthmaticus or intractable asthma, when all other methods of therapy have failed.

Treatment of Post-herpetic Neuralgia.—Dr. C. W. A. SEARLE (Putney) writes: The note on treatment of post-herpetic neuralgia ("Any Questions?" July 16, p. 216) was of great interest to me. My colleague, Dr. M. J. Duckworth, recently suggested the treatment of this condition following ophthalmic herpes by chlorpromazine tablets, 25 mg. three times a day, the patient to rest for half an hour after each tablet. Since then, between us we have treated six cases, all resistant to other forms of drug therapy. Five of these, after seven days' treatment, all admitted to considerable relief of symptoms. No additional drugs were used. The results from treatment are long nights of uninterrupted sleep, and a form of stoical euphoria with regard to the pain. The remark, "The pain is there, but it does not worry me at all, and I do not feel nearly so depressed," is typical.

OUR EXPERT replies: This response to treatment of post-herpetic neuralgia with chlorpromazine is most interesting and a similar reaction to other types of pain treated by chlorpromazine has been recorded. The drug would appear to modify the response to the pain rather than dealing with the underlying cause of the pain.

Hiatus Hernia.—Mr. R. H. FRANKLIN (London, W.12) writes: In your excellent editorial article on "Hiatus Hernia" (July 23, p. 250), I notice that you quote Ogilvie as referring to the condition as the "hole in the iron curtain." As a matter of historical accuracy I had already compared the diaphragm to the "iron curtain" in 1950 (*Ann. roy. Coll. Surg. Engl.*, 1950, **7**, 303). Also the suggestion for carrying out gastric resection for oesophagitis was made by Wangensteen in 1949 (Wangensteen, O. H., and Leven, N. L., *Surg. Gynec. Obstet.*, 1949, **88**, 560).

Post-mortem Diagnosis of Death from Air Embolism.—Professor OSCAR V. BATSON (University of Pennsylvania) writes: I should like to comment on your expert's reply ("Any Questions?" June 18, p. 1487). Air in the non-collapsible dural sinuses is a routine finding post-mortem unless the sinuses have been exposed under special conditions. Air in the (collapsible) cerebral veins enters these veins ante-mortem. My explanation, now rather generally accepted, is that the air ascends the vertebral vein complex, by-passing the pulmonary circulation. Air may or may not be found in the right heart. I have discussed this explanation,[1 2] and it has also been covered in your *Journal*[3] and elsewhere.

REFERENCES

1 *Ann. Surg.*, 1940, **112**, 138.
2 *Ann. intern. Med.*, 1942, **16**, 38.
3 *British Medical Journal*, 1951, **1**, 284.

OUR EXPERT replies: I can only repeat that, unless special care is taken in sawing through the skull, air may be drawn into the torn cerebral veins by the action of raising the calvarium, particularly if the dura is in any way adherent. Professor Batson's brilliant demonstration of the vertebral vein system has gone far to explain malignant spread from the pelvis and breast, but so far as air embolism is concerned a definite portal of entry must be established, and it is difficult to see how air could be forced into the pelvic veins during colporrhaphy.

Corrections.—In the obituary notice of the late Dr. E. A. Renner (June 4, page 1393) it was stated that Dr. Renner was the first African Director of Medical Services in any of the West African Colonies. This was incorrect, since Dr. S. L. A. Manuwa was appointed Director of Medical Services, Nigeria, in 1951, one year before Dr. Renner's appointment in Sierra Leone. Dr. S. H. O. Jones, Director of Medical Services, Gambia, was also promoted to his present appointment in 1952.

In the report of the symposium on migraine and vascular allergy held at Basle (July 30, p. 320) Professors A. Stoll and E. Rothin should have been described as being from Basle, not Zurich as stated.

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